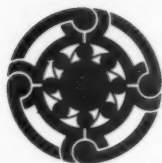


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Psychopharmacology Abstracts

U.S. DEPARTMENT
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**The U.S. Department of Health, Education, and Welfare became
the U.S. Department of Health and Human Services on May 4, 1980.**

The Secretary of Health and Human Services has determined that the publication of this periodical is necessary in the transaction of the public business required by law of this Department. Use of funds for printing this periodical has been approved by the Director of the Office of Management and Budget through November 15, 1982.

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

001001 Asano, Tomiko; Ogasawara, Nobuaki. Dept. of Biochemistry, Institute for Developmental Research, Aichi Prefecture Colony, Kasugai, Aichi 480-03, Japan **Solubilization of the benzodiazepine receptor from rat brain.** Life Sciences. 26(8):607-613, 1980.

A macromolecular moiety having high binding affinity for benzodiazepines was solubilized from a rat brain synaptosomal fraction by extraction with a combination of sodium deoxycholate and potassium chloride. This solubilized fraction exhibits pharmacological specificity for benzodiazepines. Specific 3-H-flunitrazepam binding to the solubilized fraction was saturable with the apparent dissociation constant $K_d = 1.8$ plus or minus 0.3 nM. The binding is sensitive to proteolytic enzymes. The binding is increased by GABA and decreased by inosine and hypoxanthine. These results are similar to those obtained with intact membranes, suggesting that this moiety may be the benzodiazepine receptor. The molecular weight was estimated to be approximately 200,000 by sucrose density gradient centrifugation. 17 references. (Author abstract)

001002 Axelrod, Julius. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Following the methyl group.** (Unpublished paper). Bethesda, MD, NIMH, 1979. 15 p.

Methylation reactions are discussed, including: 1) catechol-O-methyltransferase (COMT); 2) synthesis of radioactive methyl-S-adenosylmethionine and the discovery of histamine N-methyltransferase and other methyltransferases; and 3) hydroxyindole-O-methyltransferase and the pineal gland. Also discussed are: 1) phenylethanolamine N-methyltransferase (the adrenaline forming enzyme) and 2) nonspecific methyltransferase. Protein carboxymethyltransferase is detailed as well as phospholipid methylation and membrane function. 40 references.

001003 Axelrod, Julius. Section on Pharmacology, Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Phospholipid methylation and receptor mediated transmembrane signaling.** (Unpublished paper). Bethesda, MD, NIMH, 1980, 10 p.

Experiments which show that phospholipid methylation is an important receptor mediated event in the transmission of biochemical messages through membranes are reviewed. Phospholipid methylating enzymes are asymmetrically distributed in several cell membranes. During the process of methylation the lipids are translocated from the cytoplasmic side to the outside of the membrane. As phospholipids are methylated and translocated, they decrease membrane viscosity. Interaction of several ligands with cell surface receptors sets off a cascade of biochemical events initiated by increased phospholipid methylation to generate cAMP, histamine release, mitogenesis, a chemotaxis. Phospholipid methylation appears to facilitate Ca^{2+} influx which then activates phospholipase A2. The later enzyme leads to the formation of arachidonic acid and lysophosphatidylcholine. Both of these products and its many metabolites appear to be involved in the transduction of biochemical signals. Binding of ligand with its receptor stimulates phospholipid methylation in local domains of the membrane. This changes the microenvironment which then facilitates mobility of receptors and stimulates Ca^{2+} influx and phospholipase A2 and other enzymes in local areas of the membrane associated with receptors. 7 references.

001004 Axelrod, Julius; Hirata, Fusao. Section on Pharmacology, Laboratory of Clinical Science, NIMH, Bethesda, MD

20205 **Phospholipid methylation and receptor mediated transmission of biological signals through membranes.** (Unpublished paper). Bethesda, MD, NIMH, 1980. 13 p.

Experiments which show that the methylation of phospholipids are important events in the receptor mediated transmission of signals through membranes are discussed. Experiments cover: phospholipid methyltransferases and their asymmetrical distribution in membranes; phospholipid methylation and beta-adrenergic receptors; and phospholipid methylation, Ca^{2+} influx, and histamine release in mast cells. Results are also presented for experiments on: (14C)arachidonic acid release, phospholipid methylation, and cell chemotaxis; and lymphocyte mitogenesis, phospholipid methylation, and phospholipase A2 activation. The data show that many receptor mediated events such as coupling of the beta-adrenergic receptor with adenylate cyclase, histamine release by IgE antibodies, peptide activation of chemotaxis and lectin initiated mitogenesis involves methylation of membrane phospholipids. Phospholipid methylation causes changes in membrane viscosity, lipid translocation, and Ca^{2+} influx. Receptor activation of phospholipid methylation is also coupled to phospholipase A2 activation and the liberation of (14C)arachidonic acid and lysophosphatidylcholine. 19 references.

001005 Axelrod, Julius; Hirata, Fusao. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Phospholipid methylation and transduction of biochemical signals through membranes.** (Unpublished paper). Bethesda, MD, NIMH, 1980. 1 p.

Two phospholipid methyltransferases in membranes that convert phosphatidylethanolamine to phosphatidylcholine are discussed. These enzymes are asymmetrically distributed in membranes and, as they methylate phospholipids, the lipids are translocated from the cytoplasm to the outside of the membrane. In the process of methylation and translocation of the lipids membrane fluidity is increased. Interaction of beta-adrenergic receptors with their ligands in several cell types stimulates phospholipid methylation and membrane fluidity, and enhances coupling of receptor with adenylate cyclase. Desensitization of the beta-adrenergic receptor after repeated stimulation by ligands can be overcome by treatment with mepacrine, a phospholipase A2 inhibitor. Mast cells and basophils can be activated to release histamine by specific binding of IgE receptors on the cell surface. Activation of IgE receptors by IgE antigens increases phospholipid methylation, Ca^{2+} influx, metabolism of phosphatidylcholine by phospholipase A2 to lysophosphatidylcholine and arachidonic acid and histamine release. Inhibition of phospholipid methyltransferase blocks Ca^{2+} influx, phospholipase A2 activation, and histamine release by IgE antigens. Other receptor mediated events coupled to phospholipid methylation, Ca^{2+} influx, and phospholipase A2 activation involve lymphocyte mitogenesis, neutrophil chemotaxis, and stimulation of adenylate cyclase by basophils in fibroblasts. (Author abstract modified)

001006 Chavdarian, Charles G.; Castagnoli, Neal, Jr. Castagnoli: Dept. of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, CA 94143 **Synthesis, redox characteristics, and in vitro norepinephrine uptake inhibiting properties of 2-(2-mercapto-4,5-dihydroxyphenyl)ethylamine (6-mercaptodopamine).** Journal of Medicinal Chemistry. 22(11):1317-1322, 1979.

An attempt to synthesize 6-mercaptodopamine was made as part of a study of the structural features of 6-hydroxydopamine analogues associated with in vivo neuronal degeneration. Reaction conditions leading to the 1,4 addition of thiols to the model

quinone 4-methyl- α -benzoquinone were achieved, but attempts to obtain 6-thiolated dopamine analogues by this route failed. The synthesis of 6-mercaptodopamine was achieved by the regioselective thiocyanation of 0,0-dimethyldopamine, followed by bis-0-demethylation and reductive cleavage of the S-cyano group. Unlike 6-hydroxydopamine, 6-mercaptodopamine was resistant to autooxidation at pH 7.4. Cyclic voltammetric analysis indicated that electrochemically generated oxidation species of 6-mercaptodopamine are unstable and undergo spontaneous reaction, presumably intramolecular cyclization. In vivo tests showed that 6-mercaptodopamine inhibits the uptake of tritiated labeled norepinephrine by isolated rat heart atria, but to a much lesser extent than does 6-hydroxydopamine. 19 references. (Author abstract modified)

001007 Chiu, Sai-keung; Keifer, Leonard; Timberlake, Jack W. Timberlake: Dept. of Chemistry, University of New Orleans, New Orleans, LA 70122 **Synthesis of imidazolidinediones and azolidinediones from cyclization of propargylureas and propargyl carbamates.** *Journal of Medicinal Chemistry.* 22(6):746-748, 1979.

A synthetic procedure for the preparation of imidazolidinediones by the base catalyzed cyclization of propargylureas is described. This method appears to be the most versatile way of obtaining these compounds containing tertiary groups substituted on ring nitrogen number 3. One of these derivatives, 3-tert-butyl-5,5-dimethyl-2, 4-imidazolidinedione, exhibited a moderate level of subcutaneous metrazole seizure threshold activity in mice, indicates potential usefulness in the control of petit mal epileptic seizures. 22 references. (Author abstract modified)

001008 Earley, James V.; Fryer, R. Ian; Ning, Robert Y. Fryer: Dept. of Chemical Research, Hoffmann-La Roche Inc., Nutley, NJ 07110 **Quinazolines and 1,4-benzodiazepines LXXXIX: haptens useful in benzodiazepine immunoassay development.** *Journal of Pharmaceutical Sciences.* 68(7):845-850, 1979.

The syntheses of some 1,4-benzodiazepines potentially useful as haptens are described. These compounds are related to chlorazepoxide, diazepam, nitrazepam, clonazepam, and some of their metabolites. This chemistry may support the development of specific radioimmunoassays for these drugs. 20 references. (Author abstract modified)

001009 Gasco, Maria Rosa; Carlotti, Maria Eugenia. Istituto di Chimica Farmaceutica e Tossicologica dell'Universita' di Torino, Corso Raffaello 31, Turin, Italy **Kinetics of dopamine oxidation by dialkylaminoalkylphenothiazine cation radicals.** *Journal of Pharmaceutical Sciences.* 68(5):612-615, 1979.

The kinetics of dopamine oxidation by dialkylaminoalkylphenothiazine cation radicals (with two or three carbon side chains) were investigated. Results indicate that the two carbon side chain derivatives have reaction rates higher than the three carbon ones. For chlorpromazine and promazine, extrapolation of pH data showed that reaction rates become very fast at physiological pH. 25 references. (Author abstract modified)

001010 Guranowski, Andrzej B.; Chiang, Peter K.; Cantoni, Giulio L. Chiang: NIMH, Bldg. 36, Rm. 3A19, 9000 Rockville Pike, Bethesda, MD 20205 **Plant 5'-methylthioadenosine nucleosidase: purification and characterization of the enzyme from *Lupinus luteus* seeds.** (Unpublished paper). Bethesda, MD, NIMH, 1980. 32 p.

5'-Methylthioadenosine nucleosidase, the enzyme which catalyzes hydrolytic cleavage of 5'-methylthioadenosine (MeSAo) with the formation of adenine and 5-methylthioribose, has been purified to homogeneity from *Lupinus luteus* seeds by extraction

with low ionic strength buffer, ammonium sulfate fractionation, chromatography on DEAE-Sephacel, Sephadex G-200, hydroxyapatite and affinity elution from S-adenosylhomocysteine-Sepharose. The nucleosidase, $m_r=62,000$, consists of two probably identical subunits, with $m_r=31,000$ as judged by gel filtration and dodecylsulfate polyacrylamide gel electrophoresis in the presence of 2-mercaptoethanol. The enzyme shows optimum activity at pH 8.0 to 8.5 in Bicine and Hepes buffers. Compared to the bacterial nucleosidase, the plant enzyme exhibits higher specificity towards the natural substrate; the K_m for MeSAo is 4.1×10^{-5} to the minus seventh power M. Among the synthetic analogs of MeSAo tested, 11 compounds appear to be able to substitute as substrates. Furthermore, the enzyme can liberate hypoxanthine from six inosine derivatives obtained by enzymatic deamination of MeSAo and its synthetic analogs. The K_m for 5'-methylthioinosine is 5.5×10^{-5} to the minus fifth power M and the maximal velocity about 50 times lower than for MeSAo. The reaction catalyzed by the nucleosidase can be inhibited by adenine $K_i=11 \text{ mM}$, 3-deazaadenine ($K_i=\text{mM}$), and 9-erythro-(2-hydroxyl-3-nonyl)adenine ($K_i=37 \text{ mM}$). 53 references. (Author abstract modified)

001011 Hanin, Israel. Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261 **Measurement of lecithin and choline.** In: Barbeau, A., Nutrition and the brain. New York, Raven Press, 1979. Vol. 5. (p. 113-127).

Information designed to provide a schematic overview of the various necessary and available steps and approaches for the isolation and quantitative analysis of both lecithin and choline is presented. Lecithins are considered first, followed by a description of the procedures used for choline separation from tissue and its subsequent chemical analysis. An illustration of the considerations and manipulations essential for the success of the analysis is detailed. 72 references.

001012 Karoum, Farouk; Chuang, Lin-Whei; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **On the enzymatic hydrolysis of the sulfate conjugate of 3-methoxy-4-hydroxyphenylglycol (MHPG).** (Unpublished paper). Washington, DC, NIMH, 1979. 11 p.

The hydrolysis of 3-methoxy-4-hydroxyphenylglycol (MHPG) sulfate conjugate (MHPG-S04) by three enzyme preparations (crude sulfatase, pure sulfatase, and glucuronidase) was evaluated. The stability of free MHPG and MHPG-S04 to incubation with and without the three enzyme preparations was also assessed. From the results, it was concluded that free MHPG is subjected to very little or no decomposition during overnight incubation. The enzyme in the crude sulfatase from *Helix Pomatia* was found to be superior when compared to the pure sulfatase. It was further determined that 500 units of sulfatase of this enzyme preparation can completely hydrolysis 1mcg MHPG equivalent of MHPG-S04 within 1 hour at 40 degrees Celsius or overnight at minus 10 degrees Celsius. The usefulness of this unusual property is discussed. 10 references. (Author abstract)

001013 Klec, Werner A.; Streety, Richard A. Laboratory of General and Comparative Biochemistry, NIMH, Bldg 36, 3A-19, Bethesda, MD 20205 **Multiple effects of opioid-receptor interactions in a clonal cell line.** (Unpublished paper). Bethesda, MD, NIMH, 1979. 19 p.

Studies that show that clonal cell lines of neuronal origin provide opportunities to study the biochemistry of such complex behavioral phenomenon as the analgesic and addictive properties of opiates and opioid peptides are reviewed. The neuroblastoma-x-glioma NG108-15 hybrid cells, which are particularly useful

for a number of types of study because they express a variety of neuronal functions, are discussed. Opioid inhibition of adenylate cyclase, the long-term effects of opioids, and the mechanism of opioid tolerance and dependence are discussed. 44 references.

001014 Krogsgaard-Larsen, P.; Honore, T.; Hansen, J. J.; Curtis, D. R.; Lodge, D. Royal Danish School of Pharmacy, Dept. of Chemistry BC, DK-2100 Copenhagen, Denmark **New class of glutamate agonist structurally related to ibotenic acid.** *Nature*. 284(5751):64-66, 1980.

A new class of glutamate agonist obtained by structural manipulation of ibotenic acid is described. Elongation of the side chain of ibotenic acid by an additional methylene group and introduction of different ring substituents have led to isoxazole amino acids with carboxyl groups resistant to decarboxylation. A further aim of this homology was to convert the apparent L-aspartic acid agonist ibotenic acid into a glutamate agonist. The possible utility of these new compounds in pharmacological analyses of CNS glutamate receptors is noted. 31 references. (Author abstract modified)

001015 Leslie, James. School of Pharmacy, University of Maryland, Baltimore, MD 21201 **Alkaline hydrolysis of 1,3-dimethylphenobarbital.** *Journal of Pharmaceutical Sciences*. 68(5):639-642, 1979.

The reaction of 1,3-dimethylphenobarbital (DMPB) with 0.02 to 0.32M potassium hydroxide in aqueous methanol was studied. The barbiturate ring cleaved reversibly at the 1,6-position, forming a malonic acid that was stable to further hydrolysis but could readily recycle to DMPB. N,N-dimethylethylphenylmalondiamide arose from decarboxylation of the carbamic acid formed by 1,2-ring opening; this irreversible decarboxylation determined the diamide as the only final reaction product. The malonic acid, which could be isolated in solid form, appeared as N-methyl-2-phenyl-butylamide following thermal decarboxylation and degradation of the acid. The DMPB disappearance rate was biphasic, and the kinetics were consistent with the described reaction. The individual rate constants and the equilibrium constant for the reaction between DMPB, the malonic acid, and hydroxide were determined. 12 references. (Author abstract)

001016 Loew, Gilda H.; Berkowitz, Donald S. Molecular Theory Laboratory, Genetics Dept., Stanford University, Stanford, CA 94305 **Intramolecular hydrogen bonding and conformational studies of bridged thebaine and oripavine opiate narcotic agonists and antagonists.** *Journal of Medicinal Chemistry*. 22(6):603-607, 1979.

A conformational study of a series of oripavine derivatives is described. The importance of interaction between specific conformations of C19 carbinols and a lipophilic receptor site is discussed. A hypothesis is proposed to explain observed differences in pharmacological activity between diastereoisomers at C19 in the oripavine series. The influence of these diastereoisomers on the pattern of N-substituent effects on relative opiate agonist/antagonist potency is considered. 29 references. (Author abstract modified)

001017 Meek, James L. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Separation of neuropeptides by HPLC.** (Unpublished paper). Washington, DC, NIMH, 1979. 7 p.

Data are presented which show that be derived for amino acids in peptides; quantitative estimates of the hydrophobicity of the amino acids in a peptide such that its retention on high pressure liquid chromatography (HPLC) can be predicted by summing the retention coefficients for each amino acid and end

group. These data confirm the hypothesis that during separation of small peptides by HPLC, most of the amino acid residues must interact with the column matrix, and that the retention of peptides containing up to about 20 residues can be predicted solely on the basis of their amino acid composition. Predictions or isolation of metabolites or cleavage fragments, or when it is necessary to detect additional or deletion errors during synthesis. For example, in metabolic studies, estimates can be readily made of the relative elution times of many of the possible metabolites. Furthermore, the quantitative estimates of amino acid lipophilicity reported should prove useful in many other chromatographic and nonchromatographic studies. 10 references.

001018 Moody, Terry W.; Pert, Candace B. Section on Biochemistry and Pharmacology, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Endogenous bombesin-like peptides in rat brain: biochemical characterization.** (Unpublished paper). Bethesda, MD, NIMH, 1979. 16 p.

A highly specific and sensitive radioimmunoassay was developed to measure the regional distribution of bombesin-like peptides in rat brain. Extracts derived from the hypothalamus had the highest levels of bombesin-like immunoreactivity. Intermediate levels of bombesin-like immunoreactivity were observed in the thalamus and midbrain; low levels in the parietal cortex, striatum, hippocampus, and medulla pons, whereas few, if any, bombesin-like peptides were detected in the cerebellum and pituitary. Using gel filtration techniques, one major and two minor peaks of immunoreactivity were isolated from the hypothalamus, thalamus, and midbrain. It is suggested that these endogenous bombesin-like peptides may play an important neuroregulatory role in the central nervous system. 22 references. (Author abstract)

001019 no author. no address **New brain opioid suggests pituitary role in analgesia.** *Medical World News*. 21(2):29, 1980.

The discovery and partial synthesis of a new endogenous opioid named brain peptide dynorphin, is reported. The compound reportedly 200 times as potent as morphine and 50 times as powerful as beta endorphin, and its role in pain regulation, narcotic addiction, and schizophrenia is being investigated. Research indicates that the presence of dynorphin in the pituitaries of laboratory animals suggests that it may be a neurotransmitter and a circulating hormone, and that it binds specifically to receptors mediating analgesia.

001020 Paul, Hans-Helmut; Sapper, Helmut; Lohmann, Wolfgang. Institut für Biophysik der Justus-Liebig-Universität-Gießen, Leihgesterner Weg 217, D-6300 Giessen, Germany **¹H-NMR investigations of a Hammett-type substituent effect on the hydrogen bond interaction of some 1,4-benzodiazepines.** *Biochemical Pharmacology*. 29(2):137-140, 1980.

The hydrogen bond formation between some 1,4-benzodiazepines, differently substituted in positions one and seven, and the nucleobases 1-ethyl-2,4-dihydroxy-5-methylpyrimidine (eThy) and 2,4-dihydroxy-1,3-dimethylpyrimidine (mIm3Ura) has been investigated by means of proton magnetic resonance technique in chloroform solution. It has been shown that the substituents influence the thermodynamic parameters ΔH_o , ΔS_o , and ΔG_o of this interaction. The standard free energy ΔG_o correlated linearly with the Hammett substituent constant σ of the substituent in position 7 of the benzodiazepine molecule. Moreover, a correlation between the free energies of the hydrogen bond interaction and the pharmacological activities of the drugs not methylated at N-1 was found. This may indicate a possible contribution of hydrogen bonds to the molecular interaction of the 1,4-benzodiazepines at their endogenous receptor(s). 19 references. (Author abstract)

001021 Pelletier, G.; Leclerc, R.; Saavedra, J.; Brownstein, M.; Vaudry, H.; Ferland, L.; Labrie, F. MRC Group in Molecular Endocrinology, 2705 Boul. Laurier, Quebec, Canada G1V 4G2 **Origin of nerve fibers containing ACTH, beta-LPH and alpha-MSH in the rat brain. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 1 p.

Immunohistochemical techniques which involved the use of specific antibodies to adrenocorticotrophic hormone (ACTH), human or bovine beta-LPH and alpha-melanocyte stimulating hormone (alpha-MSH), and the peroxidase-antiperoxidase complex were applied to adult rats which had been deafferented 14 days before sacrifice or treated with monosodium-L-glutamate (MSG) in the neonatal period in a study of the origin of nerve fibers. After hypothalamic deafferentation, no immunoreactive fibers could be detected in extrahypothalamic areas, whereas the concentration of positive cell bodies and fibers remained unchanged within the hypothalamic island. In MSG treated animals, the arcuate nucleus was completely devoided of immunoreactive structures. A few positive cell bodies were still observed in regions lateral to the arcuate nucleus. As compared with control animals, the concentration of immunostained fibers was markedly decreased in hypothalamic and extrahypothalamic areas such as the septum, thalamus, amygdala, and periaqueductal grey. The presence of some positive fibers after destruction of the arcuate nucleus can be explained by the persistence of a few cell bodies localized in regions lateral to this nucleus. The present data strongly suggest that the cell bodies producing ACTH, beta-LPH, and alpha-MSH are located in the region of the arcuate nucleus and send axonal projections into many brain areas. (Author abstract modified)

001022 Pong, S. F.; Huang, C. L. Norwich-Eaton Pharmaceuticals, Norwich, NY 13815 **Effect of UV irradiation and tritiation on hydroxyzine.** Journal of Pharmaceutical Sciences. 68(5):666, 1979.

The effects of UV irradiation on hydroxyzine, a diphenylmethane minor tranquilizer, were examined. Results showed that hydroxyzine in aqueous solution is very unstable on UV irradiation and is also vulnerable to tritiation. In either case, p-chlorobenzophenone is a main decomposition product. 8 references.

001023 Rouot, Bruno R.; Snyder, Solomon H. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **(3H)para-amino-clonidine: a novel ligand which binds with high affinity to alpha-adrenergic receptors. (Unpublished paper).** Research Report, NIMH Grant MH-18501, 1979. 6 p.

The labeling of alpha-adrenergic binding sites in central and peripheral tissues with (3H)-para-amino-clonidine (PAC) is demonstrated, and the properties of this binding are compared to those of (3H)clonidine. (3H)PAC binds saturably with a dissociation constant of about 0.9nM to rat cerebral cortex membranes. It has about two to three times the affinity of (3H)clonidine for alpha-receptor binding sites. The greater affinity is attributable mainly to a slower dissociation of (3H)PAC than (3H)clonidine from binding sites. The relative and absolute potencies of various adrenergic agonists and antagonists in competing for (3H)PAC and (3H)clonidine binding are essentially the same. (3H)PAC can also be utilized to label alpha-adrenergic binding sites in the kidney and spleen where the relative potencies of PAC and clonidine are the same as in the brain. 22 references. (Author abstract modified)

001024 Shimazu, Takashi; Takahashi, Akira. Division of Neurochemistry, Psychiatric Research Institute of Tokyo, 2-1-8 Kamikitazawa, Setagaya-ku, Tokyo, Japan **Stimulation of hypothalamic**

ic nuclei has differential effects on lipid synthesis in brown and white adipose tissue. Nature. 284(5751):62-63, 1980.

The differential effects of electrical stimulation of hypothalamic nuclei on lipid synthesis in brown and white adipose tissue were investigated. The effects of stimulation of lateral hypothalamic (LH) nuclei and ventromedial hypothalamic nucleus (VMH) were assessed via measurement of the incorporation of tritium from 3H2O into fatty acids in vivo in rats. Electrical stimulation of the VMH enhanced fatty acid synthesis in brown adipose tissue, but not in white adipose tissue or the liver, without the intervention of insulin secretion. Electrical stimulation of the LH, however, had no appreciable effect on lipid synthesis in either type of adipose tissue. 21 references. (Author abstract modified)

001025 Simila, S.; Von Wendt, L.; Linna, S.-L. Dept. of Pediatrics, University of Oulu, Oulu, Finland **Dipropylacetate and aminoaciduria.** Journal of the Neurological Sciences. 45(1):83-86, 1980.

The effect of dipropylacetate (DPA) on amino acid levels in urine, blood plasma, and cerebrospinal fluid (CSF) was studied in 10 patients receiving DPA for epilepsy. Concentrations of amino acids were determined by an automatic amino acid analyzer. Plasma specimens were obtained after overnight fasting, and the collection of the 24 hr urine sample took place during the same day. Results show a high concentration of glycine in plasma and CSF, whereas levels of all other amino acids remained the same. The effect of DPA on urinary excretion of amino acids was of considerable significance as marked elevation of urine concentrations of alanine, asparagine, cystine, glycine, histidine, isoleucine and leucine, phenylalanine, and tyrosine were observed. It is suggested that this secondary hyperglycinemia is due to suppression of glycine conjugation reactions, whereas DPA or its metabolites might interfere with tubular reabsorption of various amino acids, thereby causing hyperaminoaciduria. 10 references. (Author abstract modified)

001026 Sprinkle, Terry Joe; Grimes, Marilyn J.; Eller, A. Gary. VA Medical Center, Neurochemistry Laboratories, Research Service (151), Augusta, GA 30904 **Isolation of 2',3'-cyclic nucleotide 3'-phosphodiesterase from human brain.** Journal of Neurochemistry. 34(4):880-887, 1980.

The isolation of the enzyme 2',3'-cyclic nucleotide 3'-phosphodiesterase from an acetone powder of human subcortical white matter is reported. The yield was about 11 mg from 28 g of powder and a specific activity of 213 unit/mg was obtained using 2',3'-cyclic CMP as the substrate. A major protein band of molecular weight approximately 96,000 was found by gel electrophoresis under nonreducing conditions. However, two distinct protein bands of molecular weight 46,000 (plus or minus 1400) and 48,000 (plus or minus 1400) were observed when the protein sample was reduced with 10 mM dithiothreitol and subjected to electrophoresis in more restrictive 12 to 15% polyacrylamide sodium dodecyl sulfate gels. This molecular weight is lower than that previously reported for the bovine enzyme. It is reported that antibodies against the purified human enzyme were raised in New Zealand white rabbits. 18 references. (Author abstract modified)

001027 Stone, Audrey L. Laboratory of Neurochemistry, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **Physical-chemical characterization of heparin fractions. (Unpublished paper).** Bethesda, MD, NIMH, 1980. 15 p.

Studies concerning the effect of molecular size on the dye binding properties of heparin active and inactive fractions are described. The metachromatic reactions of methylene blue:heparin complex were used as a means of investigating two

cation binding properties of various heparin chains, namely, regions of ordered metachromatic binding and regions of stronger metachromatic binding. A striking dependency on chain length in the ordered binding at low excess of heparin was demonstrated. The degree and stability of ordered binding increased from 6 to 20Kd, as did the biological activity of the molecular weight fractions. Fractions around 6000d or less have insufficient internal tetrasaccharides to favor the stable, ordered binding. Furthermore, the pattern seen among molecular weight fractions containing both active and inactive chains was derived from that of their active chain components, indicating that dyes might be binding preferentially to active chains in excess heparin. The increase in stability of the extrinsic Cotton effects in excess anionic sites was dramatic in active chains. It appears that the very high specific activity of the 20Kd active heparin may be related to a special structure, involving the two active tetrasaccharide groupings, which stabilizes ordered binding and creates the appropriate charge distribution for stronger interaction with antithrombin. 12 references.

001028 Tomas, Francisco; Aullo, Jose M. Departamento de Química Física, Facultad de Ciencias, Universidad de Valencia, Burjassot, Valencia, Spain **Monoamine oxidase inhibition by beta-carbolines: a quantum chemical approach.** *Journal of Pharmaceutical Sciences.* 68(6):772-776, 1979.

Monoamine oxidase inhibition by beta-carboline derivatives was studied in relation to the energy change arising from complex formation between the inhibitor and the enzyme. The energy change was expressed in terms of electronic indexes, which were estimated for a set of aromatic beta-carbolines. The electronic indexes were then correlated with experimental activity indexes by a simplified quantum chemical perturbational treatment with a multiple regression procedure. Results suggested a characteristic structure for the enzyme/inhibitor complex involving two kinds of bond; one involves the lone pyridine nitrogen pair of beta-carbolines, and the other is due to a pi-electronic interaction between the inhibitor indole fragment and a suitable area of the enzyme. This model explains the competitive inhibition by beta-carbolines compared to tryptamine and other aromatic amines that are monoamine oxidase substrates. 30 references. (Author abstract modified)

001029 Vargas, F.; Guidotti, A. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Calmodulin in brain of schizophrenics.** (Unpublished paper). Washington, DC, NIMH, 1979. 15 p.

A heat stable calcium (Ca) dependent regulator protein with the characteristics of calmodulin was extracted and purified from striatum and cerebral cortex of autopsied human brains. The human calmodulin preparation cross reacts with CA dependent phosphodiesterase isolated from rat, bovine, and human cerebral cortex. There was no significant difference between calmodulin content measured in membranes obtained from striatum or cortex of nine control subjects without a psychiatric history and seven schizophrenic individuals. 28 references. (Author abstract)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

001030 Agrawal, Devendra K.; Pandey, Bhagwan R. Dept. of Pathology and Bacteriology, King George's Medical College, University of Lucknow, Lucknow, India **Monoamine oxidase and pyruvate oxidase inhibitory properties of some newer thiosemicarbazones and their anticonvulsant activity.** *Research Communications in Chemical Pathology and Pharmacology.* 26(3):525-533, 1979.

Seventeen 4-(3-(N-cyclohexylamino)propyl)-1-substituted-3-thiosemicarbazones were synthesized and evaluated for anticon-

vulsant activity in mice and ability to inhibit rat brain monoamine oxidase (MAO) and pyruvate oxidase in vitro. The anticonvulsant activity exhibited by these thiosemicarbazones (100mg/kg i.p.) against pentylenetetrazol-induced seizures ranged from 10 to 50%. The compound with the most anticonvulsant activity showed maximum inhibition of rat brain pyruvate oxidase, while the compound with the least anticonvulsant activity provided maximum inhibition of rat brain monoamine oxidase. 10 references. (Author abstract modified)

001031 Antonini, Ippolito; Claudi, Francesco; Gulini, Ugo; Micossi, Luigi; Venturi, Fabrizio. Caludi: Istituto di Chimica Farmaceutica e di Chimica Organica, Università di Camerino, I-62032 Camerino, Italy **Indolizine derivatives with biological activity IV: 3-(2-aminoethyl)-2-methylindolizine, 3-(2-aminoethyl)-2-methyl-5,6,7,8-tetrahydroindolizine, and their N-alkyl derivatives.** *Journal of Pharmaceutical Sciences.* 68(3):321-324, 1979.

The indolizine compounds 3-(2-aminoethyl)-2-methylindolizine, 3-(2-aminoethyl)-2-methyl-5,6,7,8-tetrahydroindolizine, and some N-substituted derivatives were synthesized and tested for biological activity. Initial pharmacological screening showed that these compounds possess antiserotonergic, antihistaminic, anticholinergic, and CNS depressant properties. In general, the indolizine derivatives were more effective in inhibiting CNS activity than were the corresponding tetrahydroindolizines. 8 references. (Author abstract modified)

001032 Arnt, Jørn; Krogsgaard-Larsen, Povl. H. Lundbeck and Co. A/S, 7 Othilievej, DK-2500 Copenhagen Valby, Denmark **GABA agonists and potential antagonists related to muscimol.** *Brain Research.* 177(2):395-400, 1979.

A series of compounds structurally related to muscimol was tested for GABA agonist and antagonist activity in male Wistar rats. Intraneural injections of muscimol, dihydromuscimol, isomuscimol, and 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP) produced dose dependent contralateral turning behavior, and the drugs' potencies in eliciting turning were correlated with their affinities for GABA receptors. Contralateral turning was also elicited by 5,6,7,8-tetrahydro-4H-isoxazolo(4,5-d)azepin-3-ol (THAZ), but this effect was not dose dependent. Intraneural injections of 4,5,6,7-tetrahydroisoxazolo(3,4-c)pyridin-3-ol (isoTHIP) and 5,6,7,8-tetrahydro-4H-isoxazolo(3,4-d)azepin-3-ol (isoTHAZ) produced ipsilateral turning behavior and also antagonized the contralateral turning induced by muscimol, suggesting these agents may act as GABA antagonists. The effects of structural modifications of the muscimol molecule on GABA antagonist activity are discussed. 23 references.

001033 Atkinson, Joseph G.; Girard, Yves; Rokach, J.; Rooney, C. S.; McFarlane, C. S.; Rackham, A.; Share, N. N. Medicinal Chemistry Dept., Merck Frosst Laboratories, Pointe Claire/Dorval, Quebec, Canada H9R 4P8 **Kojic amine -- a novel gamma-aminobutyric acid analogue.** *Journal of Medicinal Chemistry.* 22(1):99-106, 1979.

A series of compounds containing the 3-hydroxy-4H-pyran-4-one nucleus was synthesized and tested for skeletal muscle relaxant activity. The most potent of the various hydroxypyrene derivatives tested was kojic amine. This GABA mimetic agent reduced flexor spasms in the chronic spinal cat preparation when administered orally or intravenously. 10 references. (Author abstract modified)

001034 Banna, N. R.; Pilcher, C. W. T. Faculty of Science, Lebanese University, Hadeth-Beirut, Lebanon **Locomotor depressant action of indole aldoloxime and its antagonism by d-amphetamine.** *Neuropharmacology.* 19(1):103-106, 1980.

Indole-3-aldehyde oxime (IAO, 25 to 150mg/kg i.p.) produced hypothermia and a profound dose related depression of locomotor activity in male MFI mice. The larger doses of IAO induced a state of total tonic immobility. Locomotor depression induced by IAO could be antagonized by pretreatment with d-amphetamine, but not by apomorphine, clonidine, imipramine, or pargyline. 6 references. (Author abstract modified)

001035 Bunce, Nigel J.; Kumar, Yogesh; Ravanal, Luis. Chemistry Dept., University of Guelph, Guelph, Ontario N1G 2W1, Canada **Phototoxicity of chlorpromazine**. *Journal of Medicinal Chemistry*. 22(2):202-204, 1979.

The constitution and decomposition of chlorpromazine was studied to determine the source of its phototoxicity. Results indicate that electron transfer from the side chain to the aromatic nucleus of the drug contributes to its instability to light. Even without the side chain, chlorophenothiazines appear to be very photolabile. It is unlikely that nonphototoxic analogues of chlorpromazine can be prepared by simply altering the constitution of the side chain. 14 references. (Author abstract modified)

001036 Cheng, Richard S. S.; Pomeranz, Bruce H. Dept. of Zoology, University of Toronto, Toronto, Ontario, Canada M5S 1A1 **Electroacupuncture analgesia is mediated by stereospecific opiate receptors and is reversed by antagonists of Type I receptors**. *Life Sciences*. 26(8):631-638, 1980.

Dextronaloxone, a recently synthesized stereoisomer, which was shown to possess much less opiate receptor affinity than levonaloxone, produces no reversal of electroacupuncture analgesia (EAA) in mice. Since levonaloxone completely reverses EAA, this proves that stereospecific opiate receptors are involved. It has been reported that there are two classes of opiate receptors: Type I and Type II. Type I opiate receptors may be responsible for opiate analgesia. Antagonism of Type I receptors, levonaloxone, naltrexone, cyclazocine, and diprenorphine, all block EAA at low doses. Results strongly support the hypothesis that EAA is mediated by opiate receptors. It is suggested that Type I receptors are the major component of this system. 14 references. (Author abstract)

001037 Clark, Judith A.; Clark, Michael S. G.; Gardner, Derek V.; Gaster, Laramie M.; Hadley, Michael S.; Miller, David; Shah, Anwer. Gardner: Beecham Pharmaceuticals Research Division, Medicinal Research Centre, Pinnacles, Harlow, Essex, CM19 5AD, England **Substituted 3-amino-1,1-diaryl-2-propanols as potential antidepressant agents**. *Journal of Medicinal Chemistry*. 22(11):1373-1379, 1979.

A series of analogues of 3-(dimethylamino)-1,1-diphenyl-2-propanol hydrobromide was synthesized and tested for potential antidepressant activity in mice. Several of these compounds prevented reserpine-induced hypothermia in mice without causing significant peripheral anticholinergic effects. The most promising compound was 1-(3-chlorophenyl)-3-(dimethylamino)-1-phenyl-2-propanol hydrochloride, which apparently potentiated the central effects of noradrenaline and 5-hydroxytryptamine. 15 references. (Author abstract modified)

001038 Clement-Cormier, Yvonne C.; Meyerson, Laurence R.; Phillips, Heidi; Davis, Virginia E. Dept. of Neurobiology, University of Texas Medical School, Houston, TX 77025 **Dopamine receptor topography: characterization of antagonist requirements of striatal dopamine-sensitive adenylate cyclase using protoberberine alkaloids**. *Biochemical Pharmacology*. 28(20):3123-3129, 1979.

Tetrahydroprotoberberines (THPB), quaternary protoberberine salts, and quaternary dehydroprotoberberine salts were used to characterize the geometric and stereospecific requirements of

antagonists of the dopamine receptor. In homogenates of male Sprague-Dawley rat caudate nucleus, (plus or minus)-2,3,10,11-THPB inhibited the ability of 100mM dopamine to elevate adenylate cyclase, and the S-(-)-isomer was a more potent antagonist of dopamine sensitive adenylate cyclase activity than the R-(-)-isomer. The positional isomer 2,3,9,10-THPB antagonized dopamine activation of adenylate cyclase with the same degree of potency as 2,3,10,11-THPB. Exhaustive O-methylation of THPB at all four hydroxyl positions response. Selective O-methylation of the THPB molecule markedly altered the potency of the resultant compounds as antagonists, depending on the position of the O-methyl substitution. Results suggests that orientation of the nitrogen atom in a fixed (cis) position two carbon atoms from a catechol nucleus contributes the antagonist properties to these compounds. 46 references. (Author abstract modified)

001039 Davis, Pamela A.; Baird-Lambert, Judith; Taylor, Kenneth M.; Maclaren, John A. Roche Research Institute of Marine Pharmacology, Dee Why, New South Wales 2099, Australia **Serotonergic activity of a novel tetrahydro-beta-carboline**. *Biochemical Pharmacology*. 28(11):1803-1806, 1979.

The synthesis and serotonergic activity of a novel tetrahydro-beta-carboline, (plus or minus) 1-ethoxycarbonylmethyl-1-methyl-1,2,3,4-tetrahydro-beta-carboline-2-ium chloride (carbonylmethyl-THBC), are described. Carbonylmethyl-THBC increased brain serotonin levels but did not inhibit monoamine oxidase activity in mice. It increased serotonin release and weakly inhibited serotonin uptake into synaptosomes prepared from rat or mouse cerebral cortex. Carbonylmethyl-THBC mimicked serotonin as an agonist on the isolated guinea-pig ileum but was 500 times less potent than serotonin. 26 references.

001040 Euvrard, C.; Ferland, L.; Di Paolo, T.; Beaulieu, M.; Labrie, F.; Oberlander, C.; Raynaud, J. P.; Boissier, J. R. Centre de Recherches Roussel-UCLAF, 102, Route de Noisy, F-93230 Romainville, France **Activity of two new potent dopaminergic agonists at the striatal and anterior pituitary levels**. *Neuropharmacology*. 19(4):379-386, 1980.

The activity of two new potent dopaminergic agonists at the striatal and anterior pituitary levels is described. Two N-diphenethylamine derivatives, RU24213 and RU24926, displaced (3H)dihydroergocryptine binding to bovine anterior pituitary membranes at KD values of 150 and 100 nM, respectively, and were potent inhibitors of prolactin release in anterior pituitary cells in primary culture at respective ED50 values of 5 and 3 nM. After administration by the oral route in the rat, both compounds exerted potent and long-lasting inhibitory effects on plasma prolactin levels which were still reduced to 45% of control 6 hours after the administration of the compound with longer lasting activity, RU24926. Furthermore, these two drugs were more potent than apomorphine in decreasing striatal dopamine turnover and increasing striatal acetylcholine levels in either intact rats or animals having a unilateral 6-hydroxy dopamine-induced lesion of the nigrostriatal dopaminergic pathway. The stimulatory effect of both RU24213 and RU24926 on striatal acetylcholine levels in intact rats was much longer lasting than that of apomorphine, a significant effect of RU24926 still being observed 4 hours after intraperitoneal administration of the compound. At concentrations up to 10 to the minus fourth power M, RU24213 and RU24926 were inactive on either basal or dopamine stimulated striatal adenylate cyclase activity. These data indicate these two new drugs have potent dopaminergic activity at the striatal and anterior pituitary levels and therefore have a potential therapeutic activity for the treatment of Parkinson's disease and prolactin secreting adenomas. 36 references. (Author abstract modified)

001041 Ginos, James Z.; Stevens, Janet M.; Nichols, David E. Dept. of Neurology, Cornell University Medical College, New York, NY 10021 **Structure-activity relationships of N-substituted dopamine and 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene analogues: behavioral effects in lesioned and reserpinized mice.** Journal of Medicinal Chemistry. 22(11):1323-1329, 1979.

N,N-disubstituted dopamine and 2-amino-6, 7-dihydroxy-1,2,3,4-tetrahydronaphthalene (6,7-ADTN) analogues were synthesized and tested for dopamine antagonism following i.p. administration to intact male Swiss mice and unilaterally caudectomized mice pretreated with reserpine or alpha-methyl-p-tyrosine. N-n-propyl N-substituted compounds were more effective than other N,N-dialkyl homologues. Of these, analogues with one alkyl group larger than propyl became inactive or showed reduced dopaminergic effects when the propyl was replaced with a larger group. The N-monosubstituted analogues showed no dopamine agonist activity. N-n-Pr-N-n-Bu-6,7-ADTN was 6 times more potent than N-n-propyl-N-phenethyl-dopamine but 10 times less potent than apomorphine. 28 references. (Author abstract modified)

001042 Hammer, R.; Berrie, C. P.; Birdsall, N. J. M.; Burgen, A. S. V.; Hulme, E. C. Dept. of Biochemistry, Dr. Karl Thomae GmbH, Biberach on the Riss, Germany **Pirenzepine distinguishes between different subclasses of muscarinic receptors.** Nature 283(5742):90-92, 1980.

Binding studies using a new antimuscarinic drug, pirenzepine, which revealed heterogeneity of binding that correlates well with the pharmacological activity are described. The binding of pirenzepine to muscarinic receptors in homogenates of several peripheral tissues and in different regions of rat brain was compared to that of a classical muscarinic antagonist, N-methylscopolamine (NMS). The in vitro binding profile of pirenzepine in the peripheral organs strikingly parallels the selectivity of the pharmacological profile of the drug, both in animal tests and in clinical trials. It is evident that pirenzepine is able to discriminate differences in the subclasses of muscarinic binding sites which are not detected by classical antagonists and which make its selective antimuscarinic action possible. 26 references. (Author abstract modified)

001043 Hester, Jackson B., Jr.; Von Voigtlander, Philip. Upjohn Company, Kalamazoo, MI 49001 **6-Aryl-4H-s-triazolo(4,3-a)(1,4)benzodiazepines. Influence of 1-substitution on pharmacological activity.** Journal of Medicinal Chemistry. 22(11):1390-1398, 1979.

A series of 1-substituted 6-aryl-4H-s-triazolo(4,3-a)(1,4)benzodiazepines was tested for CNS activity. Results showed that electronegative substituents, such as trifluoromethyl, were detrimental to activity. In contrast, many compounds with electron donating substituents at C-1 had potential therapeutic activity; in addition to showing anxiolytic potential, some were also active in animal tests used to detect antidepressant and antipsychotic activity. The properties of several analogues with 4-methyl-1-piperazinyl and 4-morpholinyl substituents at C-1 are discussed. 29 references. (Author abstract modified)

001044 Humber, Leslie G.; Bruderlein, Francois T.; Philipp, Adolf H.; Gotz, Manfred; Voith, Katherine. Voith: Dept. of Pharmacology, Ayerst Research Laboratories, Montreal, Quebec, Canada H3C 3J1 **Mapping the dopamine receptor. 1. Features derived from modifications in ring E of the neuroleptic butaclamol.** Journal of Medicinal Chemistry. 22(7):761-767, 1979.

Several analogues of butaclamol with modifications in the ring-E region of the molecule were synthesized and tested for

dopamine receptor antagonism. Two of the analogues, anhydrobutaclamol and deoxybutaclamol, exhibited neuroleptic properties as potent as those of butaclamol. An analysis of the molecular structures of the active and inactive analogues revealed the existence of a lipophilic accessory binding site on the central dopamine receptor macromolecule. The minimum dimensions of this site and its locus with respect to the primary binding sites were also determined. 37 references. (Author abstract modified)

001045 Koide, T.; Uyemura, K. Dept. of Pharmacology, Research Laboratories of Chugai Pharmaceutical Company Ltd., No. 41-8, 3-chome, Takada, Toshima-ku, Tokyo, Japan **A comparison of the inhibitory effects of new non-tricyclic amine uptake inhibitors on the uptake of norepinephrine and 5-hydroxytryptamine into synaptosomes of the rat brain.** Neuropharmacology. 19(4):349-354, 1980.

The effects of new nontricyclic amine uptake inhibitors, FS32 and FS97, on the uptake of (3H)norepinephrine (NE) into the hypothalamic synaptosomes and (3H)5-hydroxytryptamine (5-HT) into whole brain synaptosomes were studied. Their effects were compared with those of tricyclic antidepressants. The uptake of (3H)NE was inhibited competitively by FS32 and FS97 with a respective K_i value of 6.5 times 10 to the minus seventh power M and 3.8 times 10 to the minus seventh power M. The potency of FS32 and FS97 to inhibit this uptake was almost comparable to that of clomipramine and imipramine, respectively. In the case of (3H)5-HT uptake, FS32 and FS97 also showed competitive inhibition with K_i values of 2.9 times 10 to the minus sixth power M and 5.9 times 10 to the minus sixth power M. The ability of FS32 to inhibit (3H)5-HT uptake was almost equal to that of nortriptyline, while FS97 was two times more potent than iprindole in inhibiting this uptake. 28 references. (Author abstract)

001046 Kornet, Milton J.; Garrett, R. Joyce. College of Pharmacy, University of Kentucky, Lexington, KY 40506 **Synthesis of 1-phenyl-2-(phenylcarbamoyl)pyrazolidines as potential anticonvulsant agents.** Journal of Pharmaceutical Sciences. 68(3):377-378, 1979.

Twelve 1-phenyl-2-(phenylcarbamoyl)pyrazolidines were synthesized from 1-arylpyrazolidines and aryl isocyanates and tested for anticonvulsant activity. With one exception, the compounds showed no anticonvulsant activity in mice in the maximal electroshock and pentylenetetrazol seizure assays. None of the compounds showed neurotoxic effects at the three doses tested (30, 100, and 300mg/kg). 5 references. (Author abstract modified)

001047 Laduron, Pierre M.; Leysen, Josee E. Dept. of Pharmacology, Janssen Pharmaceutica, B-2340 Beerse, Belgium **Domperidone, a specific in vitro dopamine antagonist, devoid of in vivo central dopaminergic activity.** Biochemical Pharmacology. 28(14):2161-2165, 1979.

The interactions of domperidone with the dopamine receptor were studied in Wistar rats in vivo and in vitro. Domperidone was found to be a potent and specific dopamine antagonist, and (3H)domperidone binding sites were localized exclusively in homogenates of brain dopaminergic regions. However, domperidone did not exert the behavioral effects characteristics of neuroleptic drugs. A very low amount of labelling and an atypical distribution in brain after administration of (3H)domperidone suggested the drug did not penetrate into brain structures to reach the striatum. Domperidone also failed to elicit the marked increase in homovanillic acid levels observed with classical neuroleptic drugs and metoclopramide. Results suggest that domperidone does not readily cross the blood-brain barrier and

consequently has no central effects. 16 references. (Author abstract modified)

001048 Martin, Lawrence L.; Klioze, Solomon S.; Worm, Manfred; Crichlow, Charles A.; Geyer, Harry M., III; Kruse, Hansjoerg. Chemical Research Dept., Hoechst-Roussel Pharmaceuticals Inc., Somerville, NJ 08876 **Synthesis of spiro(isobenzofuran-1(3H),4'-piperidines) as potential central nervous system agents. 5. Conformationally mobile analogues derived by furan ring opening.** *Journal of Medicinal Chemistry*. 22(11):1347-1354, 1979.

A series of 4-(2-(arylmethyl)phenyl)piperidines and 4-(benzyl)-4-phenylpiperidines was synthesized and tested for potential antidepressant activity by measuring antagonism of tetrabenazine ptosis in male mice. Several of the 4-(2-(arylmethyl)phenyl)piperidines displayed antitetrabenazine activity comparable to that of imipramine or amitriptyline, but were two to four times less active than analogues 3-arylspiro(isobenzofuran-1(3H),4'-piperidines). Structure/activity relationships for 4-(2-(arylmethyl)phenyl)piperidines were generally similar to the profile established for 3-arylspiro(isobenzofuran-1(3H),4'-piperidines). Significant antitetrabenazine activity was found only in derivatives in which the arylmethyl group was ortho to the piperidine ring. The role of the furan ring in the antitetrabenazine activity of the 3-arylspiro(isobenzofuran-1(3H),4'-piperidines) is discussed. 23 references. (Author abstract modified)

001049 Mathur, K. B.; Dhotre, B. J.; Raghubir, R.; Patnaik, G. K.; Dhawan, B. N. Division of Medicinal Chemistry, Central Drug Research Institute, Lucknow 226001, India **Morphine-like activity of some new met-enkephalin analogues.** *Life Sciences*. 25(24 & 25):2023-2028, 1979.

(D-Ala², Met⁵)-Enkephalin-N-alkylamides were synthesized and tested for inhibition of electrically stimulated contraction of isolated guinea pig ileum and for analgesic activity in mice. The isopropylamide derivative had maximum activity by icv but not ip route whereas n-propylamide had similar potency by both routes and produced less respiratory depression than morphine in anesthetized cats. Factors responsible for the enhancement of analgesic activity of met-enkephalin are discussed. 20 references. (Author abstract modified)

001050 Melloni, Piero; Della Torre, Arturo; Meroni, Maurizio; Ambrosini, Anna; Rossi, Alessandro C. Carlo Erba Research Institute, I-20159 Milan, Italy **Azetidine derivatives of tricyclic antidepressant agents.** *Journal of Medicinal Chemistry*. 22(2):183-191, 1979.

Tricyclic derivatives of azetidine were synthesized and screened for their potential antidepressant activity. The active series had the tricyclic rings attached to position 1 and a basic group in position 3 of the azetidine. Results of the reserpine-induced blepharospasm and hypothermia test for antidepressant activity, Irwin's test for orientative acute toxicity, and the pentylenetetrazole test for anticonvulsant activity suggested that further research on this series of drugs is warranted. The most promising compound was (1-(6,11-dihydrodibenzol(b,e)oxepinyl)-3-(methylamino)azetidine hemifumarate, which showed CNS stimulant properties with no peripheral anticholinergic activity. 24 references. (Author abstract modified)

001051 Menon, M. Krishna; Clark, William G.; Vivonia, Charlotte. Psychopharmacology Research Laboratory, Veterans Administration Medical Center, Sepulveda, CA 91343 **Interaction between phencyclidine (PCP) and GABA-ergic drugs: clinical implications.** *Pharmacology Biochemistry and Behavior*. 12(1):113-117, 1980.

Clinical implications of the interaction between phencyclidine (PCP) and gabaergic drugs were studied. Pretreatment of mice with (-)-baclofen, muscimol, 4,5,6,7-tetrahydroisoxazolo (S,4-c) pyridin-3-ol hydrate (THIP), aminooxyacetic acid (AOAA) or gamma-acetylenic GABA caused a dose dependent inhibition of the locomotor stimulant effect of PCP. Although (-)-baclofen was found to be the most effective PCP antagonist, its () isomer was inactive. The maximum blocking effect of AOAA was seen in animals treated 3 and 6 hours earlier. Except for gamma-acetylenic GABA, none of these drugs significantly blocked the locomotor stimulant effect of d-amphetamine. Diazepam reduced d-amphetamine response, but failed to influence PCP-induced stimulation. The locomotor stimulant effect of PCP, unlike that of d-amphetamine, may be the result of a specific GABA antagonistic effect at certain dopamine rich areas of the brain. It seems that (-)-baclofen may prove to be useful in the management of PCP intoxication. Administration of higher doses of PCP (20 and 50mg/kg) in mice pretreated with (-)-baclofen resulted in the development of surgical anesthesia manifested as the loss of righting reflex, pain sensation, and corneal reflex. The duration of the general anesthetic response was found to be a function of the doses of both (-)-baclofen and PCP. The possible use of (-)-baclofen as an adjuvant to general anesthetic is discussed. 39 references. (Author abstract modified)

001052 Metcalf, Brian W. Centre de Recherche Merrell International, 16 rue d'Ankara, F-67084 Strasbourg, France **Inhibitors of GABA metabolism.** *Biochemical Pharmacology*. 28(11):1705-1712, 1979.

The development of specific inhibitors of GABA catabolism is described. The design and mechanism of action of enzyme activated enzyme inhibitors of GABA transaminase is discussed. Although the clinical utility of these substances is not yet known, these specific inhibitors of GABA metabolism should be useful in the study of GABA mediated neurotransmission. 65 references.

001053 Nagai, Yasutaka; Irie, Akira; Masuda, Yoshinobu; Oka, Makoto; Uno, Hitoshi. Research Laboratories, Dainippon Pharmaceutical Co., Ltd., 33-94, Enoki-cho, Suita, Osaka, Japan **Synthesis of 2,3,4,4a,5,9b-hexahydro-1H-pyrido(4,3-b)indole derivatives and their central nervous system activities.** *Journal of Medicinal Chemistry*. 22(6):677-683, 1979.

The synthesis and pharmacological effects of cis and trans 2-substituted 2,3,4a,5,9b-hexahydro-1H-pyrido(4,3-b)indole derivatives are described. The substituents of the 2, 5, and 8 position, together with the relative configuration of the 4a and 9b position, influenced the potency of CNS activities for these derivatives. A cis-2-(3-(p-fluorobenzoyl)propyl) analogue of carbide showed thymoleptic activity and had more potent neuroleptic activity than the parent compound in mice and rats. 16 references. (Author abstract modified)

001054 Neptune, Marilyn; McCreery, Richard L.; Manian, Albert A. McCreery: Dept. of Chemistry, Ohio State University, Columbus, OH 43210 **Electrochemical oxidation of hydroxylated phenothiazine and imipramine derivatives.** *Journal of Medicinal Chemistry*. 22(2):196-199, 1979.

The electrochemical oxidations of several hydroxylated derivatives of promazine, chlorpromazine, imipramine, and 3-chloroimipramine were compared. Oxidation of the monohydroxyphenothiazine derivatives led to both dihydroxy species and substituted benzoquinones, but oxidation of hydroxylated imipramines led to only the corresponding benzoquinones. The oxidation potentials of 17 tricyclic psychoactive drugs and metabolites are discussed in relation to drug activity and side-effects. 29 references. (Author abstract modified)

001055 Philipp, Adolf H.; Humber, Leslie G.; Voith, Katherine. Voith: Dept. of Pharmacology, Ayerst Research Laboratories, Montreal, Quebec, Canada H3C 3J1 **Mapping the dopamine receptor. 2. Features derived from modifications in the rings A/B region of the neuroleptic butaclamol.** *Journal of Medicinal Chemistry.* 22(7):768-773, 1979.

The effect of modifying the region of the butaclamol molecule occupied by rings A and B was examined, and the results were used to develop a model of the central dopamine receptor. Studies of neuroleptic activity in rats and mice indicated that the benzo(5,6)cyclohepta analogue, isobutaclamol, was equipotent to butaclamol. Analysis of the molecular structure of this compound permitted identification of a planar catechol primary binding site composed of alpha and beta regions. The minimal dimensions and locus of this site with respect to the nitrogen location site and complementary hydrogen bond donor site were also determined. 32 references. (Author abstract modified)

001056 Phillis, J. W.; Kirkpatrick, J. R. Dept. of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N 0W0 **Motilin excites neurons in the cerebral cortex and spinal cord.** *European Journal of Pharmacology.* 58(4):469-472, 1979.

As part of a survey of the effect of gastrointestinal peptides on central neurons, the 22 amino acid polypeptide motilin was tested by iontophoretic application on neurons in the male Sprague-Dawley rat cerebral cortex and by superfusion on neurons in the isolated hemisectioned toad spinal cord. Motilin excited unidentified rat corticospinal neurons and other deep spontaneously firing cortical cells. The excitation developed rapidly and lasted for up to 60 seconds after application. Motilin was also a potent excitant of neurons in the amphibian spinal cord, eliciting a depolarization of dorsal root terminals and motoneurons. Tetrodotoxin substantially reduced the effects of motilin, suggesting a primary site of action on spinal cord interneurons. 9 references. (Author abstract modified)

001057 Press, Jeffery B.; Hofmann, Corris M.; Eudy, Nancy H.; Fanshawe, William J.; Day, Ivana P.; Greenblatt, Eugene N.; Safir, Sidney R. Cardiovascular-CNS Disease Research Section, Medical Research Division, American Cyanamid Co., Lederle Laboratories, Pearl River, NY 10965 **10-(Alkylamino)-4H-thieno(3,4-b(1,5)benzodiazepines. A novel class of potential neuroleptic agents.** *Journal of Medicinal Chemistry.* 22(6):725-731, 1979.

A series of 10(alkylamino)-4H-thieno(3,4-b(1,5)benzodiazepines was synthesized and characterized pharmacologically. The effects of these compounds on d-amphetamine-induced lethality in aggregated mice and on locomotor activity in rats were used as an index of neuroleptic activity. Inhibition of tetrabenazine-induced depression in mice was used to measure antidepressant activity. Most of the compounds showed potent neuroleptic activity and several also showed antidepressant activity. It is concluded that these thienobenzodiazepines may represent a unique class of mixed action CNS agents. 10 references. (Author abstract modified)

001058 Reifenrath, William G.; Fries, David S. Fries: Unit of Medicinal and Biological Chemistry, School of Pharmacy, University of the Pacific, Stockton, CA 95211 **Aminotetralins as narcotic antagonists. Synthesis and opiate-related activity of 1-phenyl-2-aminotetralin derivatives.** *Journal of Medicinal Chemistry.* 22(2):204-206, 1979.

Three derivatives of cis-2-(methyl(cyclopropanemethyl)amino)-1-phenyltetralin were synthesized and tested for opiate agonist and antagonist activities in mice. The compounds were obtained by synthetic modification

from 2-amino-1-tetralone. In the hotplate test, c-1-phenyl-1-propionyloxy-r-2-(N-methyl-N-(cyclopropanemethyl)amino) tetralin hydrochloride was about half as potent as codeine as an analgesic. In the tail flick test, c-1-phenyl-1-methoxy-r-2-(N-methyl-N-(cyclopropanemethyl)amino)tetralin hydrochloride showed weak antagonistic activity. The compounds showed no other significant opiate related activity. 13 references. (Author abstract modified)

001059 Shankaranarayan, D.; Gopalakrishnan, C.; Kameswaran, L. Dept. of Pharmacology, Madras Medical College, Madras 600 003, S. India **Pharmacological profile of mangostin and its derivatives.** *Archives Internationales de Pharmacodynamie et de Therapie.* 239(2):257-269, 1979.

Mangostin (M) is a naturally occurring xanthone in the rinds of the fruit *Garcinia mangostana* Linn. (Guttiferae), and its derivatives 3-O-methyl mangostin (MM), 3,6-di-O-methyl mangostin (DM), 1-isomangostin (IM), mangostin triacetate (MT), mangostin 3,6-di-O-(tetra acetyl) glucoside, and mangostin-3,6-di-O-glucoside (MDG), were screened for pharmacological effects in several species. With the exception of DM, all the test compounds produced CNS depression characterized by ptosis, sedation, decreased motor activity, and potentiation of phenobarbital sleeping time and ether anesthesia in Swiss mice and Wistar rats. None of the compounds showed analgesic, antipyretic, or anticonvulsant effects. MOG produced myocardial stimulation and increased blood pressure, but the other compounds had no significant cardiovascular effects in frogs and dogs. M, IM, and MT had significant antiinflammatory activity, even in adrenalectomized rats. Antiulcer activity in rats was observed only with M. 23 references. (Author abstract modified)

001060 Sternbach, Leo H. Research Division, Hoffmann-La Roche Inc., Nutley, NJ 07110 **The benzodiazepine story.** *Journal of Medicinal Chemistry.* 22(1):1-7, 1979.

The development of the group of centrally acting 1,4-benzodiazepines is described, beginning with the discovery of chlor-diazepoxide in 1957. Structure/activity relationships are discussed, with emphasis on benzodiazepinones with substituents at the 7 or 1 position. Since all the 1,4-benzodiazepines introduced so far share muscle relaxant, sedative, anxiolytic, anticonvulsant, and hypnotic properties to varying degrees, future research is directed toward the discovery of products with a narrower spectrum of biological activities. 24 references.

001061 Tani, Junichi; Yamada, Yoshihisa; Oine, Toyonari; Ochiai, Takashi; Ishida, Ryuichi; Inoue, Ichizo. Inoue: Research Laboratories of Tanabe Seiyaku Co., Ltd., 16-89, Kashima-3-chome, Yodogawa-ku, Osaka 532, Japan **Studies on biologically active halogenated compounds. 1. Synthesis and central nervous system depressant activity of 2-(fluoromethyl)-3-aryl-4(3H)-quinazolinone derivatives.** *Journal of Medicinal Chemistry.* 22(1):95-99, 1979.

Some 2-(fluoromethyl) analogues of 2-methyl-3-aryl-4(3H)-quinazolinones were synthesized and screened for CNS activities. In general, the 2-(fluoromethyl) analogues had more potent CNS depressant activity and less toxicity than their parent compounds. It is concluded that the introduction of a fluorine atom into the 2-methyl group of 2-methyl-3-aryl-4(3H)-quinazolinones is an effective approach for exploiting the pharmacophoric effect of halogenation. 10 references. (Author abstract modified)

001062 Uno, Hitoshi; Kurokawa, Mikio; Masuda, Yoshinobu; Nishimura, Haruki. Research Laboratories, Daiinippon Pharmaceutical Company, Ltd., 33-94, Enoki-cho, Suita, Osaka, Japan **Studies on 3-substituted 1,2-benzisoxazole derivatives. 6. Syntheses of 3-(sulfamoylmethyl)-1,2-benzisoxazole derivatives and their an-**

tic convulsant activities. *Journal of Medicinal Chemistry.* 22(2):180-183, 1979.

Several 3-(sulfamoylmethyl)-1,2-benzisoxazole derivatives were synthesized from 3-(bromomethyl)-1,2-benzisoxazole by the reaction with sodium bisulfite followed by chlorination and amination. Some of these derivatives displayed marked anticonvulsant activity in mice. The introduction of a halogen atom to the 5 position of the benzisoxazole ring caused increased activity and neurotoxicity; the substitution of a sulfamoyl group caused decreased activity. The activity of monoalkylated compounds may have been the result of a biotransformation. Among these compounds, 3-(sulfamoylmethyl)-1,2-benzisoxazole appeared to be the most promising as an anticonvulsant for clinical use. 8 references. (Author abstract modified)

001063 Uwaydah, Ibrahim M.; Waddle, M. Kathleen; Rogers, Michael E. A. H. Robins Co., Richmond, VA 23220 **N-(2-cyanoethyl) derivatives of meperidine, ketobemidone, and a potent 6,7-benzomorphan.** *Journal of Medicinal Chemistry.* 22(7):889-890, 1979.

The N-(2-cyanoethyl) derivatives of meperidine, ketobemidone, and 2,5-dimethyl-9 α -ethyl-2'-hydroxy-6,7-benzomorphan were tested for antinociceptive potency and opiate receptor affinity. N-(2-cyanoethyl)-9 α -ethyl-5-methyl-6,7-benzomorphan was six times more potent than its N-methyl analogue in the hotplate assay and showed stronger receptor binding affinity in rat brain. The N-(2-cyanoethyl)-4-phenylpiperidine phenylpiperidine compounds were almost inactive compared to their N-methyl congeners. Results suggest that the pharmacological effect of the N-(2-cyanoethyl) moiety is dependent on the opioid on which it is substituted. 10 references. (Author abstract modified)

001064 Wilson, Raymond S.; May, Everett L.; Dewey, W. L. Dewey, Dept. of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Some 9-hydroxycannabinoid-like compounds. Synthesis and evaluation of analgesic and behavioral properties.** *Journal of Medicinal Chemistry.* 22(7):886-888, 1979.

A series of 9-hydroxylated cannabinoid-like compounds was prepared and tested for analgesic properties in mice and behavioral properties in dogs. Although the prototype compound, 9-nor-hydroxyhexahydrocannabinol, has potent antinociceptive activity in laboratory animals, the new analogues were relatively inactive. All of the compounds altered behavior in unanesthetized dogs; two produced cannabinoid effects and two produced general CNS depression. 16 references. (Author abstract modified)

001065 Yanagita, Tomoji; Wakasa, Yoshio; Kiyohara, Hiroko. Dept. of Psychopharmacology, Central Institute for Experimental Animals, 1433 Nogawa, Takatsu-ku, Kawasaki, 213 Japan **Drug dependence potential of viloxazine hydrochloride tested in rhesus monkeys.** *Pharmacology Biochemistry and Behavior.* 12(1):155-161, 1980.

The drug dependence potential of viloxazine hydrochloride, a recently developed antidepressant compound, was tested in five experiments with rhesus monkeys. In gross behavioral observation of normal monkeys, the acute CNS effects of the drug were found to be very weak. Decrement of spontaneous motor activity and occasional eye closing were observed with single doses higher than 16mg/kg i.v., i.m., and 128mg/kg p.o., while convulsions and death occurred at 64mg/kg i.v. and i.m. Viloxazine did not suppress the morphine and barbitol withdrawal signs in monkeys that had been made physically dependent on these drugs and withdrawn. In the test for physical dependence by repeated administration of the drug at 16mg/kg i.m. twice daily

for 31 days in normal monkeys, no observable withdrawal sign was developed in the naloxone precipitation and natural withdrawal tests. In intravenous self-administration experiments, a weak reinforcing effect was demonstrated in some monkeys, but the effect was extremely weak. Thus, viloxazine was found to be physical dependence free and its overall dependence potential is regarded as very low. 8 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

001066 Achee, Frances M.; Gabay, Sabit. Biochemical Research Laboratory, Veterans Administration Medical Center, Brockton, MA 02401 **Studies of monoamine oxidases: inhibition of bovine brain MAO in intact mitochondria by tricyclic antidepressant drugs.** *Biochemical Pharmacology.* 28(7):1197-1203, 1979.

The tricyclic antidepressant drugs (TCA) chlorimipramine, amitriptyline, desimipramine, imipramine, and doxepin reversibly inhibited monoamine oxidase (MAO) activity in intact mitochondria of beef brain cortex. Unlike the TCA inhibition reported for MAO in rabbit tissues, the inhibition observed in beef brain was greater for type-A MAO, indicated by serotonin deamination, than for type-B MAO indicated by phenylethylamine (PEA) deamination. Chlorimipramine was the most effective of the drugs tested in inhibiting serotonin deamination, and amitriptyline was the most effective in inhibiting PEA deamination. Kinetic analyses revealed marked differences in the interactions of the TCA with the type-A and type-B MAO. Combined treatment with a TCA and selective or mixed MAO inhibitor did not potentiate inhibition of MAO-A or MAO-B activity. Results suggest that MAO inhibition is of minor significance in the therapeutic efficacy of the TCAs in treating depression. 40 references. (Author abstract modified)

001067 Acheson, Ann L.; Zigmond, Michael J.; Stricker, Edward M. Dept. of Biological Sciences, University of Pittsburgh, Pittsburgh, PA 15260 **Compensatory increase in tyrosine hydroxylase activity in rat brain after intraventricular injections of 6-hydroxydopamine.** *Science.* 207(4430):537-540, 1980.

The effects of intraventricular injection of the neurotoxin 6-hydroxydopamine (6-OHDA) on norepinephrine (NE) and tyrosine hydroxylase (TH) were examined in the rat. Administration of 6-OHDA produced a permanent loss of endogenous NE and of 3H labeled NE uptake sites in the hippocampus within 5 days. These losses were initially accompanied by parallel decreases in TH activity and synaptosomal NE synthesis. Within 21 days, however, hippocampal TH activity and NE synthesis rate increased threefold to fivefold. These data suggest a novel form of plasticity in brain damaged animals characterized by an increase in the capacity for transmitter biosynthesis in residual neurons. 38 references. (Author abstract modified)

001068 Acton, George; Dailey, John W.; Morris, Stephan W.; McNatt, Laurie. Dept. of Pathology, Louisiana State University Medical School, Shreveport, LA 71130 **Evidence for an endogenous factor interfering with antagonist binding at the muscarinic cholinergic receptor.** *European Journal of Pharmacology.* 58(3):343-344, 1979.

A competitive binding assay revealed the presence of an endogenous ligand for muscarinic cholinergic receptors in several rat tissues and in fractions of whole bovine brain. The molecular weight, susceptibility to peptidase, tissue distribution, and specificity of binding to muscarinic sites were all consistent with a possible physiologic role for the endogenous muscarinic antagonist. Similar studies have demonstrated the presence of endogenous ligands at serotonergic and neuroleptic sites. 5 references.

001069 Adams, P. M. Dept. of Psychiatry and Behavioral Sciences, University of Texas Medical Branch, Galveston, TX Interaction of phencyclidine with drugs affecting cholinergic neurotransmission. *Neuropharmacology*. 19(2):151-153, 1980.

Locomotor activity induced by phencyclidine was studied in rats in combination with a number of cholinergic acting drugs (atropine, methyl atropine, and physostigmine). Atropine, but not the methyl form, potentiated the phencyclidine-induced activity. Physostigmine blocked the phencyclidine-induced activity at all dosages studied. These findings support the involvement of cholinergic receptors in the effects of phencyclidine and address several clinical pharmacology considerations in the treatment of phencyclidine toxicity. 8 references. (Author abstract)

001070 Ahnert, Gudrun; Glossmann, H.; Habermann, E. Pharmakologisches Institut der Justus Liebig-Universität Gießen, Frankfurterstrasse 107, D-6300 Lahn-Giessen 1, Germany Effects of ion channel toxins and specific neurotoxins on the cyclic nucleotide content of cerebellar slices, primary brain cultures and neural cell lines. *Naunyn-Schmiedeberg's Archives of Pharmacology*. 307(2):151-157, 1979.

Cyclic AMP and cyclic guanosine monophosphate (GMP) levels were measured in mouse cerebellar slices, neural cell lines, and primary nerve cell cultures from rats after treatment with various neurotoxins and depolarizing agents. Sea anemone toxin-II (ATXII) raised the cyclic GMP content of cerebellar slices up to 35-fold and doubled their cyclic AMP content. Mast cell degranulating peptide from bee venom increased cyclic GMP levels up to 15-fold. The effects of both ion channel toxins on cyclic nucleotide content were mimicked by high potassium and veratride. ATXII also increased cyclic nucleotide levels in 4-week-old primary nerve cultures, but not in younger cultures or in several neural lines. Specific neurotoxins-like toxin, botulinum-A toxin, and apamin from bee venom had no effect on cyclic nucleotide content of slices or cell cultures. Results suggest that toxins that open sodium channels in excitable membranes tend to raise the cyclic nucleotide content, whereas toxins that selectively attack neural constituents have no consistent effect on cyclic nucleotide levels. 33 references. (Author abstract modified)

001071 Ahnert, Gudrun; Glossmann, H.; Habermann, E. Pharmakologisches Institut der Justus Liebig-Universität Gießen, Frankfurterstrasse 107, D-6300 Lahn-Giessen 1, Germany. Investigations on the mechanism of cyclic guanosine monophosphate increase due to depolarizing agents as studied with sea anemone toxin II in mouse cerebellar slices. *Naunyn-Schmiedeberg's Archives of Pharmacology*. 307(2):159-166, 1979.

Sea anemone toxin-II (ATXII) and mast cell degranulating (MCD) peptide increased the cyclic nucleotide content in male NMRI mouse cerebellar slices. The increase in cyclic guanosine monophosphate (GMP) induced by ATXII, MCD peptide, or high potassium was diminished when sodium ions (Na) were replaced by lithium ions. Tetrodotoxin (TTX) prevented the effects of both toxins and of veratridine, but not those of high potassium. The toxin-induced accumulation of cyclic GMP was abolished in the absence of extracellular calcium ions (Ca²⁺). The so called Ca²⁺ antagonist, (-)-D-600 blocked the increase of cyclic GMP-induced by ATXII, MCD peptide, veratridine, or high potassium. ATXII stimulated the uptake of labeled Ca²⁺ in mouse cerebellar slices, and this stimulation was blocked by TTX or (-)-D-600. These findings indicate that Na influx and Ca²⁺ movement are involved in the action of ATXII and MCD peptide. 35 references. (Author abstract modified)

001072 Akasu, T.; Karczmars, A. G. Dept. of Pharmacology and Therapeutics, Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153 Effects of anticholinesterases and of sodium fluoride on neuromyal desensitization. *Neuropharmacology*. 19(4):393-403, 1980.

The effects of anticholinesterases and of sodium fluoride (NaF) on neuromyal desensitization were investigated in nerve sartorius muscle preparations of *Rana pipiens*. Desensitization was obtained by either repetitive, brief (2 msec) iontophoretic pulses of acetylcholine (ACh) or by a prolonged (40 sec) iontophoretic application of ACh. Anticholinesterase drugs, the organophosphorus tetraethylpyrophosphate (TEPP) and the carbamate, neostigmine, markedly accelerated desensitization. Data suggest that anticholinesterases exert a direct, desensitizing effect independently of the possibility of their causing accumulation of iontophoretically applied ACh. NaF employed in concentrations of 0.1 to 5 mM, significantly delayed the onset of desensitization whether the latter was induced by repetitive or prolonged pulses of ACh; it also accelerated the recovery of the endplate from desensitization. NaF also antagonized the acceleration of desensitization induced by either TEPP or neostigmine. This action occurred after prolonged TEPP treatment; thus, it is not due to the reactivating potential of NaF. Repetitive indirect stimulation of the endplate produced progressive diminution of the endplate potentials, with a plateau occurring at 60 seconds. It is emphasized that the antidesensitizing of NaF does not depend on its chelation of Ca²⁺ and that it may be due to the direct action of NaF on the receptor. 36 references. (Author abstract modified)

001073 Alderdice, Marc T. Dept. of Pharmacology, Louisiana State University Medical Center, 1542 Tulane Avenue, New Orleans, LA 70112 Physostigmine, but not neostigmine, inhibits acetylcholine release. *Brain Research*. 178(2-3):596-599, 1979.

In sciatic nerve/sartorius muscle preparations isolated from *Rana pipiens*, physostigmine not only inhibited cholinesterase activity but also decreased the amount of acetylcholine released from nerve terminals at the neuromuscular junction. Neostigmine showed only the cholinesterase inhibitory effect. A similar dual action of physostigmine on cholinesterase and on transmitter release in the CNS could account for inconsistent clinical reports of its effects in patients with Huntington's disease and tardive dyskinesia. 17 references.

001074 Alozie, Sydney O.; Martin, Billy R.; Harris, Louis S.; Dewey, William L. Dept. of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 3H-delta9-tetrahydrocannabinol, 3H-cannabinol and 3H-cannabidiol: penetration and regional distribution in rat brain. *Pharmacology Biochemistry and Behavior*. 12(2):217-221, 1980.

3H-delta9-tetrahydrocannabinol (3H-delta9-THC), 3H-cannabidiol (3H-CBD), and 3H-cannabinol (3H-CBN) were administered (1mg/kg) to male rats which were decapitated either 0.5, 1, 15, 30 or 90 minutes later. The plasma concentration was similar for all cannabinoids throughout the time course. After 5 minutes greater than 80% of the plasma radioactivity in each treatment was due to metabolites. Radioactivity rapidly entered brain after the administration of 3H-CBD, 3H-CBN, and 3H-delta9-THC. The concentrations of unchanged 3H-CBD and 3H-CBN in whole brain were higher than that of 3H-delta9-THC 5 minutes after administration. Regional distribution of radioactivity in the brain after 5 minutes was similar to all three cannabinoids, the only significant difference being in the hypothalamus. Coadministration of 3H-delta9-THC with a five fold excess of either CBD or delta9-THC did not produce any significant alteration in the levels of radioactivity in brain or plasma 5 minutes after their injection. The difference in behavior

ioral activity of delta9-THC, CBD, and CBN cannot be explained by penetrability or regional distribution in the brain. 27 references. (Author abstract)

001075 Altshuler, Harold L.; Phillips, Paul E.; Feinhandler, Donna A. Neuropsychopharmacology Section, Texas Research Institute of Mental Sciences, Houston, TX **Alteration of ethanol self-administration by naltrexone**. *Life Sciences*. 26(9):679-688, 1980.

The effect of naltrexone HCl (NLTRX) on the reinforcing properties of ethanol was evaluated with intravenous self-administration (IVSA). Eight drug naive, male rhesus monkeys were selected for: spontaneous acquisition of ethanol IVSA, consumption of at least 1.0gm/kg/day of ethanol during daily 4 hour IVSA test sessions, and extremely low daily variability (10%) of ethanol intake during a 30 day control period. The selected subject group received intramuscular injections of either saline or NLTRX 30 minutes before each test session. Saline was administered for 10 consecutive days and each NLTRX dose for 15 consecutive days. Saline phases were alternated with the NLTRX phases. NLTRX pretreatment produced lower levels of ethanol IVSA than those observed during saline pretreatment phases. The magnitude of the suppression of ethanol IVSA corresponded to NLTRX dose and was statistically significant following both 3mg/kg and 5mg/kg doses. NLTRX pretreatment produced transient increases in ethanol IVSA during the first 5 days of treatment, followed by significant decreases for the next 10 days. These data suggest that the blockade of opiate receptors by NLTRX in rhesus monkeys apparently decreases the reinforcing effects of ethanol measured with IVSA techniques. 27 references. (Author abstract modified)

001076 Amenta, F.; Bernardi, G.; Floris, V.; Marciari, M. G. Bernardi: 2 Clinica delle Malattie Nervose e Mentali, Viale dell'Università, I-30-00185 Rome, Italy **Localization of alpha-bungarotoxin binding sites within the rat corpus striatum**. *Neuropharmacology*. 18(3):319-322, 1979.

Immunofluorescence and fluorescent alpha-bungarotoxin, a potent nicotinic antagonist, were used to localize nicotinic cholinergic receptors in the corpus striatum of male Wistar rats. Few such receptors were found; the receptors were dispersed in the head of the structure and localized in a small superolateral area of the body. This finding does not support the hypothesis that acetylcholine presynaptically modulated the release of dopamine from axon terminals of the nigrostriatal projection. 19 references. (Author abstract modified)

001077 Amir, Shimon; Galina, Harold Z.; Amit, Zalman. Dept. of Psychology, H-1060, Concordia University, 1455 de Maisonneuve Blvd. W., Montreal, Quebec H3G 1M8, Canada **Chronic naltrexone administration reverses the suppressive effect of crowding on body weight gain in rats**. *Neuropharmacology*. 18(11):905-907, 1979.

The rate of body weight gain was slower in male Wistar rats maintained in crowded conditions than in those housed individually. Chronic naltrexone administration reversed the suppressive effect of crowding on body weight gain, but had no effect on body weight gain in individually housed rats. Results suggest that endogenous opioids may mediate the effect of crowding stress on appetitive behavior in rats. 16 references. (Author abstract modified)

001078 Antoniadis, A.; Muller, W. E.; Wollert, U. Pharmakologisches Institut der Universität Mainz, D-6500 Mainz, Germany **Central nervous system stimulating and depressing drugs as possible ligands of the benzodiazepine receptor**. *Neuropharmacology*. 19(1):121-124, 1980.

The interaction of several CNS stimulant and depressant drugs with the specific binding of tritiated flunitrazepam to benzodiazepine receptors in rat brain membranes was studied. Most of the anesthetic, hypnotic, anticonvulsive, and analeptic drugs tested displaced specific (3H)flunitrazepam binding at high concentrations, but only glutethimide and fominobene showed receptor affinities high enough to suggest pharmacological relevance. The respiratory stimulant fominobene showed antagonistic rather than agonistic properties at the benzodiazepine receptor. 10 references. (Author abstract modified)

001079 Antrup, Herbert; Seiler, Nikolaus. Centre de Recherche Merrell International, 16 rue d'Ankara, F-67084 Strasbourg Cedex, France **On the turnover of polyamines spermidine and spermine in mouse brain and other organs**. *Neurochemical Research*. 5(2):123-143, 1980.

The apparent biological half-lives of spermidine and spermine in mouse brain and other organs were determined by measurement of the specific radioactivities of these compounds over long periods of time. The endogenous polyamine pools were labeled by repeated intraperitoneal injections of (1,4-14C)putrescine 2HCl, (2-14C)D,L-methionine, (14C)D,L-methionine, (2-3H)L-methionine, and S-adenosyl-(2-3H)L-methionine. Repeated injections were given to ensure labeling of both fast and slow polyamine pools. It was shown that the two parts of the polyamine molecules which derive from ornithine and methionine have significantly different life spans especially in the brain. Actual turnover rates of polyamines could not be determined because of the active interconversion between spermine and spermidine, and between spermidine and putrescine. The observed reutilization of putrescine originating from spermidine degradation for spermidine biosynthesis is discussed with respect to its physiological significance and its relationship to cellular organization. 32 references. (Author abstract)

001080 Apud, J.; Cocchi, D.; Iuliano, E.; Casanueva, F.; Muller, E. E.; Racagni, G. Institute of Pharmacology, University of Milan, Via A. Del Sarto, and 21, I-20129-Milan, Italy **Determination of dopamine in the anterior pituitary as an index of tuberoinfundibular dopaminergic function**. *Brain Research*. 186(1):226-231, 1980.

Dopamine levels were determined in the anterior pituitary (AP) of rats receiving drugs capable of altering the dynamics of DA in tuberoinfundibular DA (TIDA) neurons. As a means of ascertaining that the recorded changes in AP-DA concentrations were actually reflecting alterations in DA neurotransmission, concomitant evaluation of plasma prolactin (PRL) was performed. Twenty minutes after amphetamine administration, DA concentrations in the AP were significantly increased over baseline, whereas concentrations at 10 minutes and 40 minutes were not significantly different from baseline. However, PRL in plasma showed decreases from 10 minutes up to 40 minutes. This result suggests that the amine released by amphetamine from TIDA neurons into hypophysial vessels was vehicle to and accumulated in the AP. This finding strengthens the idea that the ability of amphetamine to stimulate the release of DA into hypophysial stalk blood may be the mechanism by which this agent suppresses the release of PRL. Similar reasoning is applied to the results obtained with nomifensine and reserpine. 26 references.

001081 Ary, T. E.; Komiskey, H. L. Washington State University, College of Pharmacy, Pullman, WA 99164 **Phencyclidine: effect on the accumulation of 3H-dopamine in synaptic vesicles**. *Life Sciences*. 26(7):575-578, 1980.

The effect of phencyclidine on the accumulation of 3H-dopamine in synaptic vesicles was investigated. A subcellular frac-

tion was prepared from pig caudate by density gradient centrifugation and characterized with respect to 3H-dopamine uptake. The fraction, containing synaptic storage vesicles, was shown to be dependent upon the presence of ATP and Mg²⁺ in the incubation medium. Further, aliquots of the fraction isolated did accumulate 3H-dopamine with linearity up to an incubation time of 10 minutes. Accumulation of 3H-dopamine was inhibited by reserpine, a drug known to inhibit vesicular uptake of catecholamines. Accumulation of 3H-dopamine was reduced by the enantiomers of amphetamine. The S(-)-enantiomer was 10 times more potent than the R(-)-enantiomer. Phencyclidine was as potent as R(-)-amphetamine in reducing the accumulation of 3H-dopamine. 12 references. (Author abstract modified)

001082 Asano, Tomiko; Ogasawara, Nobuaki. Dept. of Biochemistry, Institute for Developmental Research, Aichi Prefecture Colony, Kasugai, Aichi 480-03, Japan Solubilization of gamma-aminobutyric acid receptor from rat brain. *Life Sciences*. 26(14):1131-1137, 1980.

The solubilization of gamma-aminobutyric acid (GABA) binding sites from rat brain synaptosomal fractions by extraction with a combination of sodium deoxycholate and potassium chloride was examined. Specific 3H-GABA binding to the solubilized fraction was saturable with the apparent dissociation constant, $K_d = 23.4$ plus or minus 0.2 nM. GABA agonists and an antagonist inhibited the binding. The relative potencies of these drugs in competing for 3H-GABA binding to the solubilized fraction are in good agreement with findings with the membrane fraction. It is suggested that the binding sites in the solubilized fraction retain the characteristics of membrane bound GABA receptor. 24 references. (Author abstract modified)

001083 Ashton, D.; Wauquier, A. Dept. of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium Effects of some anti-epileptic, neuroleptic and gabaminergic drugs on convulsions induced by D,L-allylglycine. *Pharmacology Biochemistry and Behavior*. 11(2):221-226, 1979.

The antagonism of various seizure and time related components of D,L-allylglycine-induced convulsions were assessed in the rat. Trimethadione and ethosuximide did not antagonize the seizure components, whereas clonazepam, phenobarbital, diphenylhydantoin, primidone, valproate sodium, aminoxycetic acid, etomidate, acetazolamide, flunarizine, pipamperone, and baclofen did. The allylglycine test may thus represent a relatively specific method of differentiating between drugs effective against partial or generalized convulsive seizures and those effective against absence seizures. Haloperidol and pimozide were completely inactive in contrast to their reported antagonism of bicuculline seizures. The spectra of active substances are discussed with respect to principal component and cluster analysis. Similarities between baclofen and etomidate, aminoxycetic acid and phenobarbital and valproate sodium, and diphenylhydantoin and flunarizine are noted. 32 references. (Author abstract modified)

001084 Bachmann, E.; Zbinden, G. Institute of Toxicology, Swiss Federal Institute of Technology, University of Zurich, Schorenstr. 16, CH-8603 Schwerzenbach, Switzerland Effect of antidepressant and neuroleptic drugs on respiratory function of rat heart mitochondria. *Biochemical Pharmacology*. 28(24):3519-3524, 1979.

The effects of five antidepressants, two phenothiazines, and one butyrophenone neuroleptic drug on respiratory functions of rat heart mitochondria were studied in vitro using four different substrates. All compounds caused uncoupling of oxidative phosphorylation with comparable no effect levels ranging from 10,000,000 to 5,000,000 moles per mg mitochondrial protein.

The uncoupling effect was accompanied by increased oxygen consumption. The same drugs were given orally twice daily to rats. Uncoupling of oxidative phosphorylation was observed in mitochondria isolated from hearts of the treated animals. Oxygen consumption was not altered. Serum and myocardial tissue levels were determined with one of the test compounds (protriptyline). Serum concentrations in rats were higher than those observed in patients treated therapeutically, but well below those observed in human overdose situations. The effects on heart mitochondria are considered to be an indicator of altered membrane functions resulting from an accumulation of the drugs in lipid membranes. 39 references. (Author abstract)

001085 Bachrach, Uriel; Benalal, Dona; Reches, Avinoam. Dept. of Molecular Biology, Hebrew University, Hadassah Medical School, Jerusalem, Israel Morphine inhibits cyclic AMP-dependent protein kinase and ornithine decarboxylase activities in neuroblastoma x glioma hybrid cells. *Life Sciences*. 25(22):1879-1883, 1979.

It is reported that the effect of morphine on neuroblastoma x glioma hybrid cells is not limited to the inhibition of adenylate cyclase activity. It is demonstrated that in morphine treated cells there is a marked reduction in the activity of both cyclic AMP-dependent protein kinase and ornithine decarboxylase in response to stimulation by prostaglandin E₁. It is suggested that the effect of morphine is to block a cascade of events which may be crucial for the normal biochemical processes in these cells. 11 references. (Author abstract)

001086 Bagchi, Sakti P.; Smith, Thomas M. Rockland Research Institute, Orangeburg, NY 10962 Synaptosomal dopamine from phenylalanine in brain: effects of some dopaminergic agents. *Research Communications in Chemical Pathology and Pharmacology*. 26(3):447-458, 1979.

Amphetamine and cogentin increased the release of dopamine formed from 14C-phenylalanine in female Wistar rat caudate nucleus synaptosomal preparation and concomitantly stimulated synthesis. Amfonelic acid also caused a net release of labeled dopamine. Reserpine markedly increased the medium level of formed dopamine but inhibited synthesis of the amine. Triton X-100 detergent almost completely inhibited the substrate uptake and the formation of dopamine. Results suggest that the synaptosomal particles represent a unit capable of synthesizing dopamine from phenylalanine. 24 references. (Author abstract modified)

001087 Bagust, J.; Kerkut, G. A. Dept. of Neurophysiology, University of Southampton, Southampton SO9 3TU, England The use of the transition elements manganese, cobalt and nickel as synaptic blocking agents on isolated, hemisected, mouse spinal cord. *Brain Research*. 182(2):474-477, 1980.

The use of manganese, cobalt, and nickel as synaptic blocking agents was examined in the isolated, hemisected mouse spinal cord. All three transition metals were effective synaptic blocking agents in the dorsal horn, but cobalt and nickel also interfered with the propagation of action potentials along the fiber tracts of the dorsal funiculus. Manganese had a much smaller effect on nerve impulse propagation; 2mM manganese chloride in combination with low calcium provided an effective means of blocking synaptic activity without significantly altering propagated activity. 4 references.

001088 Baker, Thomas; Riker, Walter F.; Zeldes, Geoffrey. Dept. of Pharmacology, Cornell University Medical College, 1300 York Avenue, New York, NY 10021 A benzodiazepine-anticholinergic drug synergism in the prevention of stress-induced gastric mucosal erosion in mice. *Journal of Clinical Pharmacology*. 19(8-9,Part1):409-414, 1979.

The effectiveness of chlorthalidone, clidinium, and a combination of the two drugs in the prevention of stress-induced gastric erosion was examined in experimentally stressed mice. Both drugs, as a function of dose were found to inhibit this stress response. Clidinium was 2.5 times more potent than chlorthalidone. The effect of one part clidinium to two parts chlorthalidone resulted in a protective effect five times greater than that for clidinium alone. This potentiation appears to be related to the ways in which combination treatment decreases autonomic input to the gastric mucosa. Thus, the peripheral cholinergic blockade by clidinium may be potentiated by a central chlorthalidone suppression of both sympathetic and parasympathetic activities. 20 references.

001089 Bakhit, Charles; Gibb, James W. Dept. of Biochemical Pharmacology and Toxicology, University of Utah, Salt Lake City, UT 84112 **In vitro effects of pH and phosphorylation on neostriatal tyrosine hydroxylase from control and haloperidol-treated rats.** *Life Sciences* 25(16):1389-1395, 1979.

Acute administration of haloperidol to male Sprague-Dawley rats produced a pH dependent decrease in the Michaelis-Menten constant (K_m) of neostriatal tyrosine hydroxylase (TH) for the pteridine cofactor 2-amino-5-hydroxy-6-methyltetrahydropterin, with no change in maximum velocity (V_{max}). The effect occurred at pH 6.5, but not at pH 6.0, pH optimum for TH. With phosphorylating conditions at pH 6.5, the haloperidol-induced activation was no longer observed and the kinetics of TH were the same as those from control rats. A significant decrease in V_{max} occurred with increasing pH from 6.0 to 6.3, but no change in K_m for cofactor was observed with increasing pH in TH from control rats. When phosphorylating conditions were employed, a marked increase in K_m for cofactor was observed; only a slight decrease in V_{max} was seen with increasing pH for the control enzyme. 21 references. (Author abstract modified)

001090 Balfour, D. J. K.; Benwell, Maureen E. M. Dept. of Pharmacology and Therapeutics, Ninewells Hospital and Medical School, Dundee, DD1 9SY, Scotland **Betamethasone-induced pituitary-adrenocortical suppression and brain 5-hydroxytryptamine in the rat.** *Psychoneuroendocrinology* 4(1):83-86, 1979.

Levels of 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) were determined in male Sprague-Dawley rat hypothalamus, hippocampus, and other brain regions following exposure to betamethasone in the drinking water over a 24 hour period. In rats killed immediately after the treatment, hippocampal 5-HT and 5-HIAA were significantly reduced; a smaller but significant reduction in 5-HIAA was also seen in the rest of the brain. In rats killed 16 hours after the withdrawal of betamethasone, only hippocampal 5-HT was significantly reduced. Betamethasone treatment did not alter hypothalamic 5-HT and 5-HIAA at either time. Plasma corticosterone and hippocampal 5-HT and 5-HIAA levels returned to their normal values within 64 hours. During this recovery period, plasma corticosterone and hippocampal 5-HT levels were significantly correlated. Results suggest that hippocampal 5-HT has a role in the feedback control of corticosterone secretion in unstressed rats. 11 references.

001091 Bannon, M. J.; Jarboe, C. H.; Carr, L. A.; Duncan, G. E. Jarboe: Dept. of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, KY 40232 **Central nervous system actions of 2,5-bis(3,4-dimethoxybenzyl)cyclopentylamine, a peripheral dopamine blocking agent.** *Life Sciences* 26(3):225-229, 1980.

The behavioral and brain catecholamine effects of 2,5-bis(3,4-dimethoxybenzyl)cyclopentylamine (DMCPA) were investigated in mice. DMCPA rapidly depleted norepinephrine. Chronic

dosing also depleted dopamine (DA), but to a lesser degree. As indicated by a lack of effect on amphetamine-induced stereotypy and apomorphine-induced emesis and failure to induce catalepsy, the compound does not block brain DA receptors. It had no effect on brain catecholamine synthesis or dopamine-beta-hydroxylase activity. It is suggested that DMCPA may prove to be of value both in the study of multiple DA receptors and in the treatment of Parkinson's disease, as one of the few drugs which will block peripheral DA-induced side-effects while allowing central D Receptor stimulation. 11 references. (Author abstract modified)

001092 Baraban, J. M.; Aghajanian, G. K. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Suppression of firing activity of 5-HT neurons in the dorsal raphe by alpha-adrenoceptor antagonists.** *Neuropharmacology* 19(4):355-363, 1980.

The suppression of firing activity of 5-HT neurons in the dorsal raphe of male Sprague-Dawley rats by a variety of alpha-adrenoceptor antagonists (WB-4101, piperoxan, thymoxamine, and phenoxybenzamine) is reported. These alpha-adrenoceptor antagonists, as well as phentolamine and dihydroergocryptine, also reduced 5-HT cell firing when applied iontophoretically. The order of potency of the drugs when applied systemically was WB-4101, piperoxan, thymoxamine, phenoxybenzamine. This ranking correlates well with their activity at classical peripheral postsynaptic alpha-adrenoceptors. In addition, the order of potency of microiontophoretically applied adrenergic agonists (norepinephrine, phenylephrine, alpha-methylnorepinephrine, isoproterenol, salbutamol) in restoring 5-HT cell firing during competitive alpha-adrenoceptor blockade suggests that this receptor should be classified in the alpha-1-adrenoceptor category. Previous anatomical studies have demonstrated that the dorsal raphe receives an adrenergic input. Taken together, these findings suggest that NE terminals, present in the dorsal raphe, mediate a tonically active adrenergic influence upon which the firing of 5-HT cells depends. 65 references. (Author abstract modified)

001093 Baring, M. D.; Walters, J. R.; Eng, N. Walters: Experimental Therapeutics Branch, NINCDS, NIH, 9000 Rockville Pike, Bethesda, MD 20205 **Action of systemic apomorphine on dopamine cell firing after neostriatal kainic acid lesion.** *Brain Research* 181(1):214-218, 1980.

The effects of unilateral injections of 2mcg kainic acid (KA) into the neostriatum of male Sprague-Dawley rats on the response of dopamine (DA) cells in the pars compacta of the substantia nigra to apomorphine were examined. The KA lesions of the striatonigral pathway did not alter the inhibitory effect of systemic apomorphine on the activity of these neurons, and haloperidol was able to reverse the effects of apomorphine in both lesioned and control animals. The KA lesion also failed to modify the inhibitory effect of apomorphine on DA synthesis. These findings indicate that apomorphine-induced inhibition of DA cell firing is not mediated by a striatonigral feedback loop. 22 references.

001094 Barker, Steven A.; Monti, John A.; Christian, Samuel T. Neurosciences Program, University of Alabama, Birmingham, AL 35294 **Metabolism of the hallucinogen N,N-dimethyltryptamine in rat brain homogenates.** *Biochemical Pharmacology* 29(7):1049-1057, 1980.

The metabolism of the hallucinogen N,N-dimethyltryptamine (DMT) in whole rat brain homogenate is reported. Metabolites of DMT were identified as indoleacetic acid, DMT-NO, N-methyltryptamine (NMT), 2-methyl-1,2,3,4-tetrahydro-beta-carboline, tryptamine, and 1,2,3,4-tetrahydro-beta-carboline. Mech-

anisms for the formation of beta-carbolines from DMT and DMT-NO are discussed. The effects of the monoamine oxidase inhibitor iproniazid phosphate on DMT metabolism were also studied. It is suggested that the reported extension of half-life and potentiation of DMT behavioral effects by iproniazid may be due to inhibition of NMT and DMT-NO formation rather than inhibition of monoamine oxidase. A cyclic pathway for the synthesis and metabolism of DMT in brain tissue is proposed. 69 references. (Author abstract modified)

001095 Barnes, C. D.; Fung, S. J.; Gintautas, J. Dept. of Physiology, Texas Tech University School of Medicine, Lubbock, TX 79430 **Brainstem noradrenergic system depression by cyclo-benzaprine**. *Neuropharmacology*. 19(2):221-224, 1980.

A possible mechanism for cyclo-benzaprine's (CBZ) depressant action on the brainstem noradrenergic system was investigated in precollicularly decerebrated cats immobilized with Flaxedil. Phenoxybenzamine (2mg/g, i.v.) was consistently observed to antagonize CBZ's suppression of both the flexor and extensor monosynaptic reflexes (MSR). Subsequent evidence for the brainstem noradrenergic system mediating the CBZ effect was established by extracellular recordings. Unitary discharges of locus ceruleus neurons identified histologically were demonstrated to be inhibited chiefly by CBZ. In some instances, the inhibition of spontaneous cerular activity was found to parallel temporally the MSR response following CBZ administration. Cerulospinal neurons characterized by physiological criteria also revealed diminished activities following CBZ. A decreased neuronal somatic excitability was also observed by the antidromically driven cerulospinal neurons following CBZ. It is concluded that CBZ's depressant action is mediated, at least in part, by the noradrenergic cerulospinal system. Other possible mechanisms of CBZ action are discussed. 16 references. (Author abstract)

001096 Barnes, Peter; Koppel, Hanno; Lewis, Paul; Hutson, Christine; Blair, Ian; Dollery, Colin. Dept. of Clinical Pharmacology, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS, England **A fluorescent analogue of propranolol does not label beta adrenoceptor sites**. *Brain Research*. 181(1):209-213, 1980.

The cerebella of male Wistar rats were examined following injection of a fluorescent analogue of propranolol, DL-9-amino-acridyl-propranolol (9-AAP, 5mg/kg) into the tail vein. The pattern of fluorescence in the cerebellum did not differ in treated and untreated animals. This finding indicates that 9-AAP, which is a potent beta-adrenoceptor antagonist in purified form, does not permit visualization of beta-adrenoceptor sites. 12 references.

001097 Baumann, P. A.; Maitre, L. Maitre: Pharmaceuticals Division, CIBA-GEIGY Ltd, CH-4002 Basel, Switzerland **Neurobiochemical aspects of maprotiline (Ludiomil) action**. *Journal of International Medical Research*. 7(5):391-400, 1979.

Neurobiochemical effects of the antidepressant drug maprotiline and results of new experiments are described. Its most obvious effect is the inhibition of noradrenaline uptake in peripheral and central neurons. The peculiarity of this action consists in its high degree of selectivity, as no inhibition of serotonin uptake could be demonstrated in vivo. The experiments show that serotonin uptake is not diminished in rat midbrain synaptosomes even after treatment with very high doses of maprotiline (600mg/kg p.o.). In addition, the influence of the antidepressant on noradrenaline and serotonin uptake was studied in rat cerebral cortex, cerebellum, hypothalamus and pons-medulla. Dopamine and serotonin uptake were measured in the corpus striatum. Again, only the uptake of noradrenaline was found to be

inhibited. There was not even a slight tendency toward inhibition of serotonin uptake. This high degree of selectivity distinguished maprotiline from the tricyclic antidepressants and thus makes it an interesting extreme type uptake inhibitor. 25 references. (Author abstract modified)

001098 Beddok, Richard A.; Mansour, Tag E. Dept. of Pharmacology, Stanford University School of Medicine, Stanford, CA 94305 **Antagonism of serotonin-activated adenylate cyclase in the liver fluke *Fasciola hepatica* by levorphanol and dextrorphan**. *Biochemical Pharmacology*. 28(24):3689-3692, 1979.

The effects of levorphanol and dextrorphan on adenylate cyclase activity was examined in cell free particles from the liver fluke, *Fasciola hepatica*. Levorphanol and dextrorphan antagonized the activation of adenylate cyclase by 5-HT. These effects were increased in the presence of naloxone. Both morphine and naloxone inhibited 5-HT stimulated adenylate cyclase activity at concentrations even higher than those for levorphanol and dextrorphan. No significant inhibition of fluoride activated cyclase by levorphanol or dextrorphan concentrations as high as 2.5mM was found. Both opiates, while acting as antagonists of 5-HT activated adenylate cyclase, also stimulated the motility of the flukes. Possible mechanisms of this nonstereospecific inhibition are discussed. 8 references.

001099 Belenky, Gregory Lucas; Holaday, John W. Dept. of Medical Neurosciences, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, DC 20012 **The opiate antagonist naloxone modifies the effects of electroconvulsive shock (ECS) on respiration, blood pressure and heart rate**. *Brain Research*. 177(2):414-417, 1979.

The effects of naloxone pretreatment on respiration, blood pressure, and heart rate following electroconvulsive shock (ECS) in male Wistar rats were determined. Naloxone hydrochloride (10mg/kg i.p.) increased respiratory rate and decreased blood pressure and heart rate following ECS. Results provide further evidence for the release of endorphins during ECS and suggest that endorphins are involved in the regulation of respiration and cardiovascular function after activation by stress. 7 references.

001100 Benninger, C.; Kadis, J.; Prince, D. A. Prince: Dept. of Neurology, Stanford University School of Medicine, Stanford, CA 94305 **Extracellular calcium and potassium changes in hippocampal slices**. *Brain Research*. 187(1):165-182, 1980.

Ca²⁺ and K⁺ ion sensitive microelectrodes were used to measure changes in ionic activities in the CA1 region of hippocampal slices during orthodromic (stratum radiatum) stimulation. Baseline levels of (K⁺) and (Ca²⁺) were those of the bathing medium which contained 5mM K⁺ and 2.0mM Ca²⁺. During stimulation (K⁺) rose to maximal levels of 12mM while (Ca²⁺) decreased to as low as 1.4mM. Systematic alterations in extracellular field potential in stratum pyramidale accompanied the ionic shifts. Following stimulation K⁺ undershoots occurred. An active K⁺ uptake mechanism was demonstrated using iontophoretic K⁺ pulses. (K⁺) and (Ca²⁺) changes occurred in parallel and in a laminar distribution with maximal changes recorded in stratum pyramidale. Maximal (K⁺) changes occurred from baselines of 5mM and declined progressively at higher baseline levels. During epileptiform activity produced by exposure of slices to penicillin, larger ionic shifts with a more rapid onset occurred. The alterations in (K⁺) and (Ca²⁺) in the hippocampal slice are similar in some respects to those obtained by stimulation in vivo, making this preparation a potentially useful one for determination of mechanisms and effects of alterations in the ionic microenvironment. 50 references. (Author abstract)

001101 Bereiter, David A.; Barker, David J. Barker: Dept. of Physiology, North Texas State University Health Sciences

Center, Camp Bowie at Montgomery, Fort Worth, TX 76107 **Hormone-induced enlargement of receptive fields in trigeminal mechanoreceptive neurons. I. Time course, hormone, sex and modality specificity.** Brain Research. 184(2):395-410, 1980.

The phenomenon of hormone-induced enlargement of receptive field area in mechanoreceptive neurons was investigated with respect to time course, hormone, sex, and modality specificity. It was found that hormone-induced receptive field enlargement appears specific for estrogen. Castrated male rats treated for 10 days with estradiol benzoate (EB) show the same increase in receptive field area as females. Analysis of receptive field area as a function of receptive field type and adaptation rate shows that EB-induced field area enlargement is specific to rapidly adapting mechanoreceptive neurons. 43 references. (Author abstract modified)

001102 Bereiter, David A.; Stanford, Larry R.; Barker, David J. Barker: Dept. of Physiology, North Texas State University Health Sciences, Camp Bowie at Montgomery, Fort Worth, TX 76107 **Hormone-induced enlargement of receptive fields in trigeminal mechanoreceptive neurons. II. Possible mechanisms.** Brain Research. 184(2):411-423, 1980.

Several possible mechanisms to account for hormone-induced enlargement of receptive field areas of individual mechanoreceptive trigeminal neurons of the rat were investigated. Mechanoreceptor sensitivity was estimated by receptive field thresholds and showed no consistent change following systemic estrogen treatment. Alteration of the viscoelastic properties of skin was suggested as 10 days of estrogen treatment caused an acute epidermal hyperplasia, (38.7%), but force displacement measurements revealed no significant change in skin distensibility. Both chemical (6-hydroxydopamine) and surgical sympathectomy mimicked the effect of estrogen on receptive field areas by promoting dramatic enlargement of individual neuronal fields without decreasing receptive field force thresholds. Among skin samples from estrogen, 6-hydroxydopamine and surgical sympathectomized animals, only 6-hydroxydopamine treatment caused any significant alteration in skin norepinephrine content. These results strongly suggest an indirect catecholamine involvement in estrogen-induced enlargement of receptive field areas. 28 references. (Author abstract)

001103 Bernthal, Patricia J.; Koss, Michael C. University of Oklahoma, Health Sciences Center, College of Medicine, Dept. of Pharmacology, P. O. Box 26901, Oklahoma City, OK 73190 **Effects of clonidine and chlorpromazine on a sympathetic-cholinergic reflex.** European Journal of Pharmacology. 60(1):23-29, 1979.

Intravenous administration of clonidine and chlorpromazine resulted in a dose dependent inhibition of the amplitude of reflexly evoked electrodermal responses in intact and spinal cats. Pretreatment with yohimbine (0.5mg/kg i.v.) antagonized the effects of clonidine in both preparations, but did not alter those of chlorpromazine. Results suggest that clonidine and chlorpromazine act through different mechanisms to inhibit the amplitude of centrally evoked responses in this sympathetic cholinergic system. 33 references. (Author abstract modified)

001104 Bhargava, Hemendra N. Dept. of Pharmacognosy and Pharmacology, University of Illinois at the Medical Center, Chicago, IL 60612 **The effects of thyrotropin releasing hormone and histidyl-proline diketopiperazine on delta9-tetrahydrocannabinol-induced hypothermia.** Life Sciences. 26(11):845-850, 1980.

The effects of central and peripheral administration of thyrotropin releasing hormone (TRH) and its postulated metabolite, histidyl-proline diketopiperazine (HPD) on delta9-tetrahydrocannabinol (delta9-THC) induced hypothermia in

mice were investigated. Intraperitoneal administration of delta9-THC produced hypothermia, with peak response between 1 and 2 hours postinjection and with duration of 5 to 6 hours. Intracerebral or intraperitoneal administration of TRH prior to the delta9-THC injection antagonized the hypothermic response of the latter. Similar effects were produced by HPD given intracerebrally. However, HPD was completely ineffective when given intraperitoneally. The antagonism of delta9-THC-induced hypothermia by TRH may be mediated by its conversion to HPD in the CNS. 20 references. (Author abstract modified)

001105 Bhargava, Hemendra N.; Walter, Roderich; Ritzmann, Ronald F. Dept. of Pharmacognosy and Pharmacology, University of Illinois at the Medical Center, Chicago, IL 60612 **Development of narcotic tolerance and physical dependence: effects of Pro-Leu-Gly-NH2 and cyclo (Leu-Gly).** Pharmacology Biochemistry and Behavior. 12(1):73-77, 1980.

The inhibition of the development of tolerance to and physical dependence on morphine (induced via pellet implantation) by administration of Pro-Leu-Gly-NH2 (MIF) and cyclo (Leu-Gly) is reported. Inhibition of tolerance development by peptides was evidenced by the presence of an analgesic response (increase in jump threshold) as determined by measuring the jump threshold to an increasing electric current, after a challenge dose of morphine (40mg/kg). The same dose of morphine did not alter the jump threshold in morphine tolerant mice which were injected with saline prior to pellet implantation. The inhibition of the development of physical dependence on morphine by these peptides was evidenced by the antagonism of the hypothermic response which occurs during abrupt or naloxone-induced withdrawal. The naloxone-induced withdrawal jumping response was unaffected by these peptides. Dose-response experiments indicated that cyclo (Leu-Gly) was much more potent than MIF in these tests. These peptides, when given after the development of tolerance and dependence, did not modify either the analgesic response to morphine or the symptoms of abrupt and naloxone precipitated withdrawal. The inhibition of development of analgesic tolerance and physical dependence was not associated with changes in brain morphine concentrations. Data indicate that these peptides do not interfere with the morphine/morphine receptor complex formation but alter a subsequent step in the genesis of some aspects of tolerance and dependence processes. 12 references. (Author abstract modified)

001106 Bianchi, Clementina; Tanganelli, Sergio; Beani, Lorenzo. Dept. of Pharmacology and Pharmacognosy, University of Ferrara, Via Fossato di Mortara 23, Ferrara, Italy **Dopamine modulation of acetylcholine release from the guinea-pig brain.** European Journal of Pharmacology. 58(3):235-246, 1979.

The effects of dopamine (DA) and apomorphine (APO) on the release of acetylcholine (ACh) from guinea-pig brain were examined in vitro and in vivo. DA reduced the release of ACh from slices of caudate nucleus, and APO reduced ACh release from the caudate and the cerebral cortex; neither DA nor APO affected ACh release from tuberculum olfactorium or brainstem. The DA and APO inhibition of ACh release in caudate nucleus was antagonized by spiroperidol. Intracerebroventricular (i.c.v.) injection of DA (1.5 and 5mcmoles) in unrestrained rats caused a delayed, moderate behavioral stimulation and enhanced ACh outflow from the parietal cortex; i.c.v. or i.p. injection APO elicited similar effects. Spiroperidol (0.5 to 32mg/kg i.p.) counteracted behavioral stimulation induced by APO or amphetamine, but enhanced cortical ACh outflow; cholinergic responses to APO or amphetamine were unaffected. Results indicate that DA directly inhibits ACh release from striatal cholinergic structures in vitro via classical neuroleptic sensitive receptors. The enhanced cortical ACh outflow caused by DA in un-

anesthetized animals suggests a disinhibition of corticopetal cholinergic neurons via a neuroleptic insensitive mechanism. Thus, the paradoxical effect of spiroperidol may represent the consequence of increased activity of nigral DA cells with collaterals possibly involved in the control of ascending cholinergic pathways. 39 references. (Author abstract modified)

001107 Bickel, M. Abt. Pharmakologie, Hoechst Aktiengesellschaft, D-6230 Frankfurt/Main 80, Germany **Antilucer effects of nomifensine, a new antidepressant, on stress-induced ulcers in the rat.** *Arzneimittel Forschung*. 30(1):69-73, 1980.

The effectiveness of the antidepressant agents 8-amino-1,2,3,4-tetrahydro-2-methyl-4-phenyl-isoquinoline (nomifensine) and amitriptyline on various ulcer models was tested using at least 300 rats. Oral application of 3mg/kg nomifensine resulted in a 50% decrease of stress ulcers produced by water immersion. Using an immobilization ulcer model, the ID₅₀ of nomifensine was calculated to be 1.89mg/kg p.o. Amitriptyline proved to be less active in both models. Neither of the two compounds had any beneficial effects on ulcers produced by pyloric ligation. Gastric acid secretion stimulated with either histamine or penta-gastrin was not affected by nomifensine. Thus, peripheral gastric effects of nomifensine could be ruled out; its antilucer properties may be of central origin, possibly via noradrenergic mechanisms in the hypothalamus. 56 references. (Author abstract modified)

001108 Biegion, Anat; Samuel, David. Isotope Dept., Weizmann Institute of Science, Rehovot, Israel **Interaction of tricyclic antidepressants with opiate receptors.** *Biochemical Pharmacology*. 29(3):460-462, 1980.

The ability of tricyclic antidepressants to displace the specific binding of 3H-naloxone in a crude membrane preparation from rat brain was examined. All of the antidepressants tested (desipramine, amitriptyline, milserine, fluoxetine, nortriptyline, imipramine, doxepin, and dibenzepine) were capable of a complete displacement of the specific binding of naloxone. All the tricyclics had very similar IC₅₀ values between 21 and 34 μM. The nortriptyline had a lower affinity. In addition, desipramine and amitriptyline were tested for their analgesic action in adult female rats receiving increasing shock intensities. For both drugs, the pain threshold rose in proportion to the dose. The analgesic effect was completely antagonized by an i.p. injection of 2mg/kg naloxone. It is suggested that the interaction of antidepressants with the opiate receptors may account not only for their analgesic effect, but also for part of their antidepressant effect. 17 references.

001109 Blennow, Gosta; Folbergrova, Jaroslava; Nilsson, Bengt; Siesjö, Bo K. Laboratory of Experimental Brain Research, E-blocket, University Hospital, Lund, Sweden **Cerebral metabolic and circulatory changes in the rat during sustained seizures induced by DL-homocysteine.** *Brain Research*. 179(1):129-146, 1979.

Cerebral metabolic and circulatory changes were studied during sustained, generalized seizure activity induced by DL-homocysteine thiolactone (11mmol/kg i.p.) in anesthetized, paralyzed, artificially ventilated male Wistar rats. Epileptic discharges in the EEG were accompanied by marked perturbation of tissue metabolites, including a fall in phosphocreatine concentration to 40% of control, moderate changes in adenine nucleotides, a marked rise in lactate concentration, and a pronounced increase in the lactate/pyruvate ratio. Excessive amounts of dihydroxyacetone phosphate and glyceraldehyde phosphate accumulated. A marked accumulation of ammonia, glutamine, and alanine and a reduction in glutamate and aspartate concentrations were observed. Administration of a subconvulsive dose of homocysteine (7.5mmol/kg) produced changes in ammonia and

amino acids qualitatively similar to those seen during seizures. It is concluded that changes in metabolites of the energy reserve were mainly caused by the induced seizures, while those affecting amino acid concentrations were significantly influenced by accumulation of ammonia, secondary to metabolism of injected homocysteine. Cerebral oxygen utilization rose to 150% of control during sustained seizures, with a corresponding increase in cerebral blood flow. 38 references. (Author abstract modified)

001110 Blinn, G.; Heinz, G.; Jurna, I. Institut für Pharmakologie und Toxikologie der Universität des Saarlandes, D-665 Homburg/Saar, Germany **Effects of substantia nigra stimulation on suralis-evoked spinal reflex activity: comparison with the effects of morphine and stimulation in the periaqueductal gray matter.** *Neuropharmacology*. 19(1):75-85, 1980.

The effects of morphine and of conditioning stimulation of the substantia nigra (SN) or periaqueductal gray matter (PAG) on spinal reflex activity in Wistar rats were compared. In spinal rats, morphine (2mg/kg i.v.) did not significantly affect the ventral root short latency reflex response to sural nerve stimulation, but depressed the long latency reflex response. Naloxone (0.2mg/kg i.v.) abolished this depressant effect of morphine. In rats with pre-nigral decerebration, trains of conditioning stimuli delivered to the SN or PAG enhanced the short latency reflex response to sural nerve stimulation, depressed the long latency reflex response to stimulation of the skin nerve, and evoked potentials in ventral and dorsal roots. The effects of stimulation of the SN or PAG were markedly reduced by lesions of the dorso-lateral funiculi. Morphine enhanced the potentials evoked in ventral and dorsal roots by brainstem stimulation with short trains of impulses, but not with long trains. In rats with pre-nigral decerebration, SN stimulation depressed the C-fiber evoked long latency reflex response, suggesting that the SN inhibits transmission of nociceptive impulses in the rat spinal cord. 62 references. (Author abstract modified)

001111 Bloom, Alan S.; Kiernan, Cecilia J. Dept. of Pharmacology, Medical College of Wisconsin, P.O. Box 26509, Milwaukee, WI 53226 **Interaction of ambient temperature with the effects of delta-9-tetrahydrocannabinol on brain catecholamine synthesis and plasma corticosterone levels.** *Psychopharmacology*. 67(3):215-219, 1980.

The effects of delta 9 = tetrahydrocannabinol (THC) on body temperature, catecholamine synthesis and plasma corticosteroid levels were examined in the mouse at ambient temperatures of 31 degrees, 20 degrees, and 10 degrees C, to study the role of hypothermia in THC's other actions. THC produced hypothermia at 10 degrees and 20 degrees C, but not at 31 degrees C. Dose related increases in dopamine and norepinephrine synthesis rates and plasma corticosterone levels were produced by THC at both 31 degrees and 20 degrees C. The effects of THC at 10 degrees C were biphasic. These data indicate that the effects of THC on brain catecholamines are not a result of drug-induced hypothermia and may be a result of a direct action on neurons. 25 references. (Author abstract)

001112 Boadle-Biber, Margaret C. Dept. of Physiology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Activation of tryptophan hydroxylase from slices of rat brain stem incubated with agents which promote calcium uptake or intraneuronal release.** *Biochemical Pharmacology*. 28(14):2129-2138, 1979.

Incubation of slices of male Sprague-Dawley rat brainstem under conditions that promote calcium accumulation by nerve tissue or intraneuronal release of calcium from mitochondrial stores produced an increase in the activity of tryptophan hydroxylase prepared from the slices. The increase in enzyme ac-

tivity following treatment of the slices with sodium free medium, ouabain, ionophore A23187, guanidine, cyanide, or azide was reflected in altered kinetic properties of the enzyme; the Michaelis-Menten constant value of the enzyme for both substrate and artificial reduced pterin cofactor was decreased, and the maximum velocity was modestly increased. No increase in enzyme activity was observed when calcium ions were omitted from the sodium free medium and media containing ouabain or A23187. Removal of external calcium did not abolish the increase in enzyme activity obtained with metabolic inhibitors, presumably because these substances release calcium from mitochondria. Results are consistent with the view that an increase in free intraneuronal calcium triggers certain biochemical events that activate tryptophan hydroxylase. 82 references. (Author abstract modified)

001113 Boarder, Michael R.; Fillenz, Marianne. Dept. of Psychiatry, Stanford University Medical Center, Stanford, CA 94305 **The induction of tyrosine hydroxylase in terminals of noradrenergic neurons in the rat brain: studies with synaptosomal preparations.** *Journal of Neurochemistry.* 34(4):1016-1018, 1980.

The functional consequences of tyrosine hydroxylase induction following the administration of reserpine in the rat were investigated. There was no effect of reserpine compared with saline on the activity of tyrosine hydroxylase in intact synaptosomes from either hippocampus or hypothalamus. When dibutyryl cyclic AMP and tetrahydrobiopterin were added to synaptosomal preparations from both saline and reserpine pretreated animals, the cyclic AMP elevation of hippocampal synaptosomal tyrosine hydroxylation activity in the saline group failed to reach the level of significance. Otherwise, cyclic AMP elevated tyrosine hydroxylation rates from both hippocampal and hypothalamic preparations and tetrahydrobiopterin elevated activity in the hypothalamic but not hippocampal preparations. Results are discussed in terms of the regulatory process which maintains the level of hydroxylation at a constant rate. It is concluded that neither cyclic AMP availability nor biopterin levels are the regulatory processes involved in preventing the expression of the elevated enzyme levels in the hypothalamic preparations from the reserpine pretreated group. 14 references.

001114 Borbe, Harald O.; Muller, Walter E.; Wollert, Uwe. *Pharmakologisches Institut der Universität Mainz, D-6500 Mainz, Germany* **The identification of benzodiazepine receptors with brain-like specificity in bovine retina.** *Brain Research.* 182(2):466-469, 1980.

Benzodiazepine receptor binding was demonstrated in crude homogenates of bovine retina. Specific (3H)flunitrazepam binding was saturable with half maximal binding at about 5nM, but nonspecific binding increased linearly with total (3H)flunitrazepam concentration. At 0.5nM (3H)flunitrazepam, specific binding accounted for 20 to 40% of total binding. Scatchard analysis of these data revealed a single population of binding sites, with a dissociation constant of about 6nM and a maximal number of binding sites of about 0.4pmol/mg protein. The pharmacological specificity of these sites was similar to that of brain benzodiazepine receptors, but the overall density of benzodiazepine receptors was much lower in bovine retina than in rat brain. 14 references.

001115 Boulton, Alan A.; Dyck, Lillian E. *Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan, Canada S7N 0X0* **The effect of reserpine on the amine-induced release of tritiated meta-tyramine, para-tyramine and dopamine from slices of rat striatum.** *Research Communications in Psychopharmacology, Psychiatry and Behavior.* 5(1):79-94, 1980.

The effect of reserpine on the amine-induced release of tritiated meta-tyramine (m-TA), para-tyramine (p-TA), and dopamine (DA) from slices of rat striatum was investigated. Slices of rat striatum were preloaded by incubation with tritiated m-TA, p-TA or DA. The unlabeled amines were able to release a portion of the accumulated tritiated amines. The releasing abilities of the unlabeled amines were very similar. Reserpine reduced the uptake of all three labeled amines and had a differential effect on the releasing abilities of the three unlabeled amines. Reserpine had no effect on the amine-induced releases of m-TA, but potentiated the amine-induced releases of DA. In the case of p-TA, reserpine had different effects with each unlabeled amine. It was concluded that the amine/amine interaction is complex. It is evident, however, that the three amines behave differentially depending on their location and their identity. 16 references. (Author abstract modified)

001116 Bowery, N. G.; Hill, D. R.; Hudson, A. L.; Doble, A.; Middlemiss, D. N.; Shaw, J.; Turnbull, M. *Dept. of Pharmacology, St. Thomas' Hospital Medical School, London SE1, England (-)* **Baclofen decreases neurotransmitter release in the mammalian CNS by an action at a novel GABA receptor.** *Nature.* 283(5742):92-94, 1980.

The presence of a novel GABA receptor within the mammalian CNS and its action in the (-)baclofen induced decrease in neurotransmitter release in the mammalian CNS are described. Slices of CNS tissue were allowed to accumulate radiolabelled transmitter, and the effect of GABA and its analogues on the basal and K evoked release into fresh superfusion fluid was assessed. Three areas of the rat CNS were chosen, the cerebellum, striatum, and frontal cortex. Findings suggest that baclofen may mimic the action of GABA at a novel site on nerve terminals. Despite failure to obtain an antagonist for this receptor, observations of cross-desensitization, lack of additivity with supramaximal doses, and parallelism of log dose response curves in peripheral models indicate that baclofen and GABA act on the same site. As (-)baclofen is the active isomer not only at this receptor but also in producing neuronal depression, its mechanism of action in the therapy of spasticity may indeed be linked with GABA. 37 references. (Author abstract modified)

001117 Bremer, Alfonso M.; Yamada, Kazuo; West, Charles R. *Dept. of Neurosurgery, University Hospital of Jacksonville, 655 West Eighth Street, Jacksonville, FL 32209* **Ischemic cerebral edema in primates: effects of acetazolamide, phenytoin, sorbitol, dexamethasone, and methylprednisolone on brain water and electrolytes.** *Neurosurgery.* 6(2):149-154, 1980.

The effects of acetazolamide, phenytoin, sorbitol, dexamethasone, and methylprednisolone on brain water and electrolytes in primates with ischemic cerebral edema were investigated. Brain edema was induced in primates (*Macaca mulatta*) after regional cerebral ischemia produced by selective embolization of the internal carotid artery bifurcation. Acetazolamide failed to improve ischemic edema and, rather, increased mortality. Phenytoin definitely prevented both edema and infarction in only the cerebral cortex. Sorbitol was effective to induce dehydration of the affected cortex and the normal brain tissue, with obvious reduction of the brain bulk. High dose steroids showed an ability to modify edema in the cortex, putamen, and white matter. However, animals treated with methylprednisolone rather than dexamethasone showed a better neurological recovery and smaller infarcts. 43 references. (Author abstract modified)

001118 Broch, Ole Jacob. *Dept. of Pharmacology, University of Bergen Medical School, N-5016 Haukeland sykehus, Bergen, Norway* **In vivo effects of benzotropine and nomifensine on dopamine and noradrenaline terminals in rat brain.** *European Journal of Pharmacology.* 58(4):419-424, 1979.

Two weeks after intracerebroventricular administration of 200mcg 6-hydroxydopamine (6-OHDA) to male Wistar rats, dopamine in the corpus striatum and noradrenaline in the rest of the forebrain were reduced to 46% and 23% of control values, respectively. Intraperitoneal pretreatment with nomifensine (10mg/kg), desipramine (25mg/kg), or amphetamine (5mg/kg) prevented the depletion of noradrenaline, and nomifensine also had some effect when given after 6-OHDA. Nomifensine and amphetamine both altered dopamine content when given before or after 6-OHDA, but desipramine had no effect on dopamine content. A large dose of benzotropine (25mg/kg) had a small effect on dopamine when given after 6-OHDA and none when given before the neurotoxin. 15 references. (Author abstract modified)

001119 Brodie, Marjorie E.; Laverty, Richard; McQueen, Ewen G. M.R.C. Toxicology Research Unit, University of Otago Medical School, P.O. Box 913, Dunedin, New Zealand **Effect of probenecid on mouse brain tyrosine hydroxylase activity and catecholamines.** *Neuropharmacology*. 19(1):129-131, 1980.

Tyrosine hydroxylase activity and catecholamine levels were measured in four brain regions 35 to 45 minutes after i.p. administration of 200mg/kg probenecid to male mice. Tyrosine hydroxylase activity was significantly reduced in the striatum and noradrenaline levels were significantly elevated in the brainstem. Results suggest that probenecid induced elevation of acidic monoamine metabolites in the brain produces a decrease in central neuronal activity that may lead to changes in catecholamine turnover and behavior. 10 references. (Author abstract modified)

001120 Brown, D. R.; Growdon, J. H. Growdon: Dept. of Neurology, Tufts-New England Medical Center Hospital, Boston, MA 02111 **L-Tryptophan administration potentiates serotonin-dependent myoclonic behavior in the rat.** *Neuropharmacology*. 19(4):343-347, 1980.

The effects of L-tryptophan (L-TP) administration on the serotonin dependent postural myoclonic syndrome produced in rats by ip injection of p-chloroamphetamine (PCA) were investigated via administration of 10mcg/kg PCA to separate groups of rats pretreated with either 50mcg/kg of L-TP, a suspension of neutral amino acids with L-TP excluded, or saline. The postural syndrome was graded visually on a zero to 20 point scale and the animals were killed 1 to 2 hours after PCA injections. Tryptophan administration increased whole brain tryptophan levels 100%, increased brain and spinal cord indoleamine levels 66%, and enhanced PCA induced myoclonic behavior 34% compared to saline controls. In separate experiments, spinal cords were transected in nine rats and intercollicular decerebrations made in five rats. Subsequent injections of 10mcg/kg of PCA produced myoclonus in both groups, although other features of the postural syndrome did not occur in most decerebrate animals. It is concluded from these experiments that tryptophan induced increases in brain and spinal cord serotonin content enhance behaviors that depend on serotonin release, and that the myoclonus induced by PCA is not abolished by acute intercollicular decerebration or spinal cord transection. 21 references. (Author abstract modified)

001121 Brown, Harold; Uphouse, Lynda. Dept. of Psychology, Yale University, New Haven, CT 06520 **Corticosterone effects on rat brain template active region chromatin.** *Pharmacology Biochemistry and Behavior*. 12(2):207-212, 1980.

The effect of prenatal exposure to corticosterone on brain chromatin was examined. Pregnant Fischer inbred rats were administered corticosterone or saline on days 17 and 18 of gestation and their offspring examined at birth or at 2, 3, 4, or 6 days

of age. In utero exposure to corticosterone was associated with a 24 hour delay of a developmental peak in the percentage of brain template active region chromatin. Brain and body weights of the steroid and saline treated animals were similar, but corticosterone led to a temporary decrease in body and brain weight at 2 days of age which was reversed at 6 days of age. These results suggest an impact of corticosterone on brain gene expression. 30 references. (Author abstract)

001122 Brown, Lucy L.; Makman, Maynard H.; Wolfson, Leslie I.; Dvorkin, B.; Warner, Carolyn; Katzman, Robert. Dept. of Neurology, Albert Einstein College of Medicine, Bronx, NY 10461 **A direct role of dopamine in the rat subthalamic nucleus and an adjacent intrapeduncular area.** *Science*. 206(4425):1416-1418, 1979.

The role of dopamine in the rat subthalamic nucleus and an adjacent intrapeduncular area was investigated. It was found that the subthalamic nucleus, a clinically important component of the extrapyramidal motor system, and a lateral area extending into the peduncle contain catecholamine terminal and dopamine receptors coupled to adenylate cyclase. In addition, dopamine agonists administered in vivo enhance glucose utilization in the region. Thus, neuronal function in this region is directly affected by dopamine and dopaminergic drugs. 17 references. (Author abstract modified)

001123 Broxterman, Henk J.; Noach, Erik L.; Van Valkenburg, Cees F. M. Leiden University Medical Center, Dept. of Pharmacology, Sylvius Laboratories, Wassenaarseweg 72, 2333 AL Leyden, The Netherlands **Differential effects of acute and subacute HA-966 treatment on storage and release of striatal dopamine.** *European Journal of Pharmacology*. 60(2/3):153-161, 1979.

Acute injections of 1-hydroxy-3-amino-pyrrolidone-2 (HA-966, 100mg/kg i.p.) caused a rapid elevation of dopamine (DA) in the striatum of male Wistar rats. Levels of 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) increased after a latency period of 0.5 hour and 1 hour, respectively. Repeated HA-966 treatment produced smaller DA increases than acute administration, but metabolite levels increased similarly after the two treatments. No alteration in the DA increase induced by subacute HA-966 treatment was seen 1 hour after lesion of the nigrostriatal pathway. HA-966 prevented the disappearance of DA after synthesis inhibition with alpha-methyl-p-tyrosine for about 3 hours, but did not alter the decline of DOPAC and HVA after monoamine oxidase inhibition. It is concluded that HA-966 acts on the storage mechanism for newly formed DA. 40 references. (Author abstract modified)

001124 Bruns, R. F.; Pons, F.; Daly, J. W. Laboratory of Bioorganic Chemistry, National Institute of Arthritis, Metabolism, and Digestive Diseases, NIH, Bethesda, MD 20205 **Glutamate- and veratridine-elicited accumulations of cyclic AMP in brain slices: a role for factors which potentiate adenosine-responsive systems.** *Brain Research*. 189(2):550-555, 1980.

The possible role of factors other than adenosine in the response of cyclic 3',5'-adenosine monophosphate (cAMP) systems to glutamate and depolarizing agents was investigated using guinea-pig cerebral cortical slices in the presence of adenosine deaminase. A deaminase resistant analog, 2-chloroadenosine, was used to activate adenosine systems and thus detect factors which might function only via potentiation of adenosine sensitive cAMP systems. Results indicate that glutamate and veratridine elicit accumulation of cAMP in brain slices primarily by facilitating adenosine dependent activation of cAMP generating systems via release of some unknown regulatory factor(s). It is noted that the unknown factors released by depolarizing agents

or glutamate which have no effects except to potentiate adenosine elicited accumulations of cAMP in brain slices appear particularly relevant to the role of adenosine in the CNS. 23 references.

001125 Bugajski, J.; Zacny, E.; Zdebska, A. Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland **The involvement of central alpha-adrenergic and histamine H2-receptors in the hypothermia induced by clonidine in the rat.** *Neuropharmacology*. 19(1):9-15, 1980.

Clonidine (50mcg/kg) injected i.p. into male Wistar rats induced a significant decrease in body temperature lasting for 3 hours, with maximum effect 1 hour after administration. The hypothermic response to clonidine was not modified by 30 minute pretreatment with the alpha-adrenergic antagonist phentolamine (1mg/kg i.p.), the beta-adrenergic antagonist propranolol (3mg/kg i.p.), or the histamine H2 receptor antagonist cimetidine (25 to 50mg/kg i.p.). However, the hypothermic response to clonidine was antagonized by up to 81% by intracerebroventricular (i.c.v.) injection of phentolamine (5 to 10mcg) 15 minutes prior to clonidine. Phentolamine also antagonized the hyperthermic response to i.c.v. noradrenaline. Propranolol (50mcg i.c.v.) did not influence the clonidine induced hypothermia. Cimetidine (25 to 50mcg i.c.v.) abolished up to 72% of the hypothermic response to clonidine, but did not alter the hypothermic response to noradrenaline. 33 references. (Author abstract modified)

001126 Burke, David H.; Brooks, Jack C.; Ryan, Robert P.; Trembl, Susan B. Dept. of Basic Science, Division of Pharmacology, Marquette University, School of Dentistry, 604 North 16th St., Milwaukee, WI 53233 **p-Chloroamphetamine antagonism of cobaltous chloride-induced hypothermia in mice.** *European Journal of Pharmacology*. 60(2/3):241-243, 1979.

The effect of pretreatment with p-chloroamphetamine hydrochloride (PCA) on the body temperature response to cobaltous chloride was examined in male Swiss mice. A 44% reduction in brain serotonin was observed 2 hours after i.p. injection of 10mg/kg PCA, but no significant change was observed 10 days after PCA. The hypothermia induced by 25mg/kg i.p. cobaltous chloride was reduced by about 60% in PCA pretreated animals, presumably as a result of serotonin depletion. 7 references. (Author abstract modified)

001127 Bustamante, L.; Lueders, H.; Pippenger, C.; Goldensohn, E. S. Dept. de Fisiologia, Facultad de Medicina, Universidad de Zulia, Apartado 15158, Maracaibo, Venezuela **Effects of phenytoin on the penicillin-induced spike focus.** *Electroencephalography and Clinical Neurophysiology*. 48(1):90-97, 1980.

The effects of phenytoin on penicillin induce spike foci were evaluated quantitatively in cats. At blood levels considered within the therapeutic range in humans, phenytoin decreased spike duration and abolished afterdischarges. Spiking at weak foci was completely abolished by high concentrations of phenytoin. It is concluded that phenytoin primarily affects the long chain pathways. 17 references.

001128 Buzas, Andre; Champagnac, Andre; Dehnel, Andre; Lavielle, Gilbert; Pommier, Michele. Laboratoire de Synthèse Organique, UER Sciences, Université d'Orléans, 45045, Orléans, France **Synthesis and psychoanalytic properties of new compounds structurally related to diphenhydramine.** *Journal of Medicinal Chemistry*. 23(2):149-153, 1980.

A new series of benzhydryloxyalkylpiperazines carrying a trivalent function has been synthesized and studied for its effect on the CNS. Most of the compounds exhibit unexpected nonam-

phetaminic psychoanalytic properties. The structure activity studies reveal the importance of the nature and the position of the substituents on the phenyl rings. However, no significant correlation between atropinic or antihistaminic effects and psychoanalytic properties was observed. 15 references. (Author abstract)

001129 Cameron, Oliver G.; Smith, Charles B. Dept. of Psychiatry, University of Michigan, Ann Arbor, MI 48109 **Comparison of acute and chronic lithium treatment on 3H-norepinephrine uptake by rat brain slices.** *Psychopharmacology*. 67(1):81-85, 1980.

The effects of lithium chloride, given i.p. in high and low doses twice daily, upon 3H-norepinephrine uptake and retention were examined with slices from four regions of the rat brain: brainstem, hypothalamus, parietal cortex, and caudate nucleus. Control uptake was significantly higher in slices from the caudate nucleus and lower in brainstem slices than in slices from hypothalamus or parietal cortex. With the higher doses, uptake was increased after 7 days but normal at 14 days. Only in caudate slices was there a second elevation of 3H-norepinephrine uptake after 21 days of treatment, which returned to normal by 42 days. No other effects were observed during 70 days of treatment with lithium. The correlation between changes in 3H-norepinephrine uptake and plasma lithium levels was studied. 23 references. (Author abstract modified)

001130 Carey, Russell G.; Bear, Mark F.; Diamond, Irving T. Division of Neurobiology, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, AZ 85013 **The laminar organization of the reciprocal projections between the claustrum and striate cortex in the tree shrew, Tupaia glis.** *Brain Research*. 184(1):193-198, 1980.

The laminar organization of the reciprocal projections between the claustrum and striate cortex in the tree shrew, Tupaia glis, was examined by the methods of anterograde as well as retrograde transport. Reciprocal connections between the claustrum and striate cortex were shown by comparing the results after injections of horseradish peroxidase (HRP) with the results from injections of tritiated amino acids in striate cortex. The descending cortical projection originates in layer VI. The ascending projection from the claustrum terminates in every layer that receives ascending thalamo-cortical projections, being heaviest in layer IV. The organization, in which the projections from the claustrum overlap that of the geniculo-striate system as well as the projection from the intralaminar nuclei to striate cortex, places the claustrum in the unique position of being capable of modifying all ascending visual input from thalamus to striate cortex. 23 references.

001131 Chan, Arthur W. K.; Schanley, Donna L.; Strauss, William. Research Institute on Alcoholism, Buffalo, NY 14203 **The combined effect of chlordiazepoxide and ethanol on brain gamma aminobutyric acid levels.** *Research Communications in Psychology, Psychiatry and Behavior*. 4(3):277-284, 1979.

The combined effect of chlordiazepoxide (CDP) and ethanol on the contents of gamma aminobutyric acid (GABA) in various brain regions of male mice was investigated to determine if a supra additive effect on the alterations of GABA levels occurred. Findings showed that mice injected with saline/ethanol were found to have significantly elevated GABA levels in various brain regions. On the other hand, mice injected with CDP/saline had significantly lower GABA levels in the cerebrum at .25 and 2 hours and in the cerebellum 2 hours after the second saline injection. Those receiving the combination of CDP/ethanol did not have significantly different GABA levels from those receiving only saline/ethanol. An analysis of variance re-

vealed no significant interaction effect in the mice treated with the combination, indicating that no supra additive effect on the alterations of GABA levels occurred. 17 references. (Author abstract modified)

001132 Chance, William T.; White, Alice C.; Krynock, Glenn M.; Rosecrans, John A. Dept. of Pharmacology, N.E. Ohio Universities College of Medicine, Rootstown, OH 44272 **Autoanalgesia: acquisition, blockade and relationship to opiate binding.** European Journal of Pharmacology. 58(4):461-468, 1979.

In male Sprague-Dawley rats that were shocked 10 seconds after the determination of tail flick latencies each day for 7 days, autoanalgesia was acquired by the second fear conditioning trial. Pretreatment with naltrexone or diazepam had no effect, but spinal cord transection at the thoracic level blocked the autoanalgesia. Opiate and opioid binding studies showed significantly less binding in the fear conditioned rats than in controls and revealed an inverse relationship between binding and antinociception. Results suggest that autoanalgesia is mediated in part by an endogenous opioid peptide that is released by the fear conditioning procedure. 31 references. (Author abstract modified)

001133 Chang, Raymond S. L.; Snyder, Solomon H. Snyder: Dept. of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Histamine H1-receptor binding sites in guinea pig brain membranes: regulation of agonist interactions by guanine nucleotides and cations.** Journal of Neurochemistry. 34(4):916-922, 1980.

The effects of sodium, divalent cations, and guanine nucleotides on agonist and antagonist interactions with histamine H1-receptors were investigated. Agonist, but not antagonist interactions were found to be regulated selectively by these agents. Sodium decreased the affinity of histamine and the agonist 2-aminoethylpyridine for (3H)mepyramine sites in guinea pig brain membranes up to tenfold; the same effect was exerted to a lesser extent by lithium, while potassium and rubidium were much weaker. Guanine nucleotides also decreased the affinity of histamine for H1 binding sites about twofold. GTP and its non-metabolized analogue GMP-PNP as well as GDP exerted similar effects, while GMP, ATP, ADP, and AMP were inactive. Manganese was the most potent enhancer of histamine at H1-receptors, while magnesium was almost as active and calcium was essentially inactive. It is reported that sodium, divalent cations, and guanine nucleotides have negligible effects on the interactions of antihistamines with H1-receptors. 37 references. (Author abstract modified)

001134 Chapleam, Charles E.; White, Richard P.; Robertson, James T. White: Dept. of Pharmacology, University of Tennessee Center for the Health Sciences, Memphis, TN 38163 **Cerebral vasospasm: effects of prostaglandin synthetase inhibitors in vitro.** Neurosurgery. 6(2):155-159, 1980.

The direct effects of arachidonic acid, the precursor of prostaglandins (PGs), on isolated dog basilar arteries were examined, and the actions of three PG synthesis inhibitors, aspirin, indomethacin, and meclofenamate, on contractions induced by agonists of diverse chemical structure were investigated. Arachidonic acid induced sustained contractions and in optimal concentrations produced constriction that was 56% as great as that produced by serotonin. These responses were markedly inhibited (95%) by meclofenamate, but aspirin had no such effect. Moreover, meclofenamate reduced resting tension and inhibited by 16% the optimal responses caused by PGF₂alpha, while having no significant effect on serotonin contractions. Higher doses of meclofenamate (10 raised to the minus third or fourth power M) produced increasing degrees of inhibition of contractions caused by serotonin or PGF₂alpha. Conversely, aspirin

had no effect on PGF₂alpha contractions and slightly enhanced serotonin effects. The actions of indomethacin resembled those of meclofenamate. Results show clearly that different prostaglandin synthesis inhibitors have different effects on cerebral vasomotion in vitro. Aspirin, known to inhibit platelet function markedly, seems to have little effect on isolated vascular smooth muscle. It is suggested that the pharmacodynamic affects of meclofenamate and some related drugs may afford a new approach in the treatment of cerebral vasospasm. 28 references. (Author abstract modified)

001135 Chatelain, Pierre; Reckinger, Nicole; Roncucci, Romeo. Continental Pharma Research Laboratories, Machehen, Belgium **Effect of sulcotidil on Na/K ATPase activity and on membrane fluidity in rat brain synaptosomes.** Biochemical Pharmacology. 28(24):3677-3680, 1979.

The effects of sulcotidil, chlorpromazine, and ouabain on Na/K ATPase activity and on membrane fluidity were studied in rat brain synaptosomes. Sulcotidil appeared to be a potent inhibitor of the Na/K ATPase, inhibiting activity of the enzyme by 50% at 3.10 to 5 M. At this concentration, chlorpromazine and ouabain inhibited the hydrolysis of ATP by 20% and 55%, respectively. The variation of fluidity and the enzymatic inhibition were related with a correlation coefficient of .996 for sulcotidil and .965 for chlorpromazine. Two compounds related to sulcotidil, CP-1136-S and CP-894-S, were also tested. Implications of findings are discussed in terms of an electrostatic interaction of sulcotidil with acidic phospholipids in the lipid matrix. 21 references.

001136 Chen, Fon-Chiu Mia; Yamamura, Henry I.; Roeske, William R. Roeske: Dept. of Internal Medicine, Arizona Health Sciences Center, Tucson, AZ 85724 **Ontogeny of mammalian myocardial beta-adrenergic receptors.** European Journal of Pharmacology. 58(3):255-264, 1979.

Beta-adrenergic receptors were identified and characterized in fetal, neonatal, and adult mouse heart, using tritiated (3H)-(-)-dihydroalprenolol (3H-DHA). Hearts from 21 day fetal mouse responded to (-)-isoproterenol with a doubling of heart rate, but 13 day fetal mouse hearts (FMH) in organ culture were insensitive to the drug. The beta-adrenergic receptor densities, expressed as a percentage of adult receptor density, were 14% in 13 day FMH, 29% in 15 day FMH, 41% in 17 day FMH, 65% in 19 day FMH, 73% in 21 day FMH, 93% for 1 day neonate heart, 168% for 3 day neonates, and 173% for 14 day neonates. The affinity of the beta-adrenergic receptors did not change during development. Results suggest that the beta-adrenergic receptor appears prior to detectable heart rate response, increases significantly during the third trimester, and dramatically increases in the postnatal period before declining to adult level. 23 references. (Author abstract modified)

001137 Cheng, Richard S. S.; Pomeranz, Bruce. Zoology Dept., University of Toronto, Toronto, Ontario M5S 1A1. Canada **Correlation of genetic differences in endorphin systems with analgesic effects of D-amino acids in mice.** Brain Research. 177(3):583-587, 1979.

The analgesic effects of D-phenylalanine and D-leucine (D-amino acids, D-AAs) were tested in three strains of mice, selected for elevated levels of pituitary endorphins (Ob/Ob), low levels of opiate receptors (CXBK), or predicted, the D-AAs produced a more potent naloxone reversible analgesia in the Ob/Ob mice than in the B6AF1/J mice and showed no analgesic effects in the CXBK mice. These findings confirm the role of endorphins in the analgesia induced by the D-AAs and suggest that the D-AAs may prove to be potent, nonaddictive analgesics suitable for human use. 12 references.

001138 Cherubini, E.; Anchors, J. M. III Cattedra di Neuropsichiatria Infantile, c/o Istituto di Medicina Legale, Viale Regina Elena 336, I-00185 Rome, Italy **Effects of nigral and cortical stimulation on cyclic AMP in the caudate nucleus of the cat.** *Neuropharmacology*. 19(1):111-115, 1980.

The effects of cortical (CX) and nigral (SN) stimulation of cyclic AMP in the caudate nucleus (CD) were compared in intact cats and cats with unilateral lesions of the medial forebrain bundle. After unilateral stimulation of both SN and CS in intact cats, cyclic AMP increased significantly in the CD of the stimulated side. In unilaterally lesioned cats, no increase in cyclic AMP was detected in the CD of the lesioned side after bilateral SN and CX stimulation. Results suggest that the stimulation induced increase in cyclic AMP in the CD may involve a dopaminergic input. 14 references. (Author abstract modified)

001139 Chiang, Peter K.; Im, Young S.; Cantoni, Giulio L. Laboratory of General and Comparative Biochemistry, NIMH, Bethesda, MD 20205 **Phospholipids biosynthesis by methylations and choline incorporation: effect of 3-deazaadenosine.** (Unpublished paper). Bethesda, MD, NIMH, 1979. 18 p.

Data are presented to show that methylation of phospholipids or phosphatidylethanolamine *in vivo* is greatly reduced in livers of rats or hamsters treated with 3-deazaadenosine. However, it was found that the absolute amounts of phospholipids and phosphatidylcholine remained constant between the livers of control and treated animals. Concomitant with the inhibition of phospholipids methylation, there was a drastic increase in the incorporation of choline into phosphatidylcholine or phospholipids fractions. In the rat liver, the rate of uptake of choline was apparently determined by its utilization for phosphatidylcholine biosynthesis. These observations suggest intricate control mechanisms regulating phospholipids biosynthesis between methylation pathway and incorporation from choline. In the hamster liver, where 3-deazaadenosylhomocysteine is the major nucleosidylhomocysteine present after administration of 3-deazaadenosine, it is apparent that 3-deazaadenosylhomocysteine exerts an inhibitory potency similar to that of adenosylhomocysteine. 25 references. (Author abstract)

001140 Chiu, Ted H.; Rosenberg, Howard C. Dept. of Pharmacology, Medical College of Ohio, Toledo, OH 43699 **Differential effects of Triton X-100 on benzodiazepine and GABA binding in a frozen-thawed synaptosomal fraction of rat brain.** *European Journal of Pharmacology*. 58(3):335-338, 1979.

The effects of Triton X-100, a mild nonionic detergent, on the binding of tritiated GABA and diazepam was measured in a frozen/thawed synaptosomal fraction of male Sprague-Dawley rat brain. The specific binding of both ligands was increased by the detergent. Increasing concentrations of Triton X-100 progressively decreased diazepam binding capacity but first increased, then decreased GABA binding. Diazepam binding affinity was not altered by Triton X-100, but GABA binding affinity increased. It is concluded that Triton X-100 preferentially solubilizes benzodiazepine binding, indicating that GABA and benzodiazepine binding sites are on separate macromolecules. 10 references. (Author abstract modified)

001141 Christian, Samuel T. University of Alabama, Birmingham, AL 35233 **The effect of drugs of abuse on synaptic membranes.** (Unpublished paper). Final Report, NIMH Grant R01-MH-24177, 1979. 9 p.

Rat brains were used in the characterization of the effects of the four major classes of drugs of abuse on the magnesium (Mg) dependent adenosine triphosphate (ATP) associated with synaptic vesicles. A flow dialysis system developed for a direct *in vitro* study of the parameters involved in the mechanism of

transmitter release from neuronal vesicle was used in the study. The interaction of the four major transmitters with their corresponding high affinity binding sites on synaptosomal membranes is characterized, and the effect of drugs of abuse on these processes are described. The interaction of drugs of abuse with isolated synaptosomal membranes is characterized in terms of membrane structural perturbations as determined by fluorescent probe techniques. 9 references.

001142 Chuang, De-Maw; Kinnier, William J.; Farber, Len; Costa, Erminio. Costa: Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **A biochemical study of receptor internalization during beta adrenergic receptor desensitization in frog erythrocytes.** (Unpublished paper). Washington, DC, NIMH, 1980. 37 p.

Frog erythrocytes were incubated with labeled (hydroxybenzylisoproterenol), a potent agonist for beta-adrenergic receptors in a followup study of data which suggest that the recognition sites of beta-adrenergic receptors located in the plasma membrane internalize following a persistent receptor stimulation. The results suggest that the agonist is bound to the internalized recognition sites of beta-adrenergic receptors. The increase in the number of receptors found in cytosol and the decrease of those found in the particular fraction was inhibited by lowering the preincubation temperature. The binding capacity of these internalized sites was blocked by pronase but was resistant to phospholipase treatment. Dinitrophenol and Cordycepin inhibited the agonist-elicited internalization of beta-adrenergic receptors, suggesting that protein phosphorylation or other ATP-requiring metabolic processes may participate in causing this event. Preincubation of cells with concanavalin-A at dose that induce erythrocyte agglutination was found to inhibit the agonist-induced internalization. Pretreatment with methylamine in mM ranges also reduced the extent of beta-receptor internalization. 36 references. (Author abstract modified)

001143 Chung Hwang, Eunyong; Van Woert, Melvin H. Dept. of Neurology, Mount Sinai School of Medicine, Fifth Avenue and 100th St., New York, NY 10029 **Antimyoclonic action of clonazepam: the role of serotonin.** *European Journal of Pharmacology*. 60(1):31-40, 1979.

Clonazepam (2mg/kg) reduced p,p'-DDT-induced myoclonus in mice by 50%. This antimyoclonic action of clonazepam was counteracted by the serotonin (5-HT) receptor blockers methysergide, metergoline, and cinnanserin and was potentiated by the 5-HT uptake inhibitors fluoxetine and chlorimipramine. Clonazepam (4mg/kg) reduced plasma tryptophan by 27%, but had no effect on brain tryptophan, 5-HT, 5-hydroxyindoleacetic acid, 5-HT synthesis, or tritiated 5-HT, receptor binding. Clonazepam inhibited brain synaptosomal 3H-5-HT uptake and increased 3H-5-HT release *in vitro*, but had no effect on 5-HT uptake and release *in vivo*. The GABA agonists muscimol, acetylenic GABA, and amino-oxyacetic acid and the GABA antagonists bicuculline did not contract the antimyoclonic effect of clonazepam. Results suggest that the antimyoclonic action of clonazepam is mediated by enhancement of serotonergic transmission rather than through GABA mechanisms. 38 references. (Author abstract modified)

001144 Church, G. A.; Kimelberg, H. K.; Sapirstein, V. S. Kimelberg: Division of Neurosurgery, Albany Medical College, Albany, NY 12208 **Stimulation of carbonic anhydrase activity and phosphorylation in primary astroglial cultures by norepinephrine.** *Journal of Neurochemistry*. 34(4):873-879, 1980.

The effects of norepinephrine (NE) and histamine on carbonic anhydrase activity in primary astroglial cultures started from the dissociated cerebral hemispheres of neonatal rats were studied.

Carbonic anhydrase activity was increased up to twofold after treatment with 0.1 mM norepinephrine or histamine. The carbonic anhydrase activity of primary cultures derived from the cerebellum plus brainstem regions was about fourfold greater than the activity of primary cultures started from cerebral hemispheres, but in contrast was not stimulated by norepinephrine. Treatment of the cerebral cultures with norepinephrine in the presence of 32P resulted in a two to threefold increased incorporation of 32P into carbonic anhydrase purified from the same cultures, and this increased incorporation was inhibited by propranolol. It is suggested that one of the consequences of the stimulation of 3',5'-cyclic AMP levels in brain by norepinephrine is activation of astroglial carbonic anhydrase activity due to 3',5'-cyclic AMP stimulated phosphorylation of the enzyme. 36 references. (Author abstract modified)

001145 Clarke, G.; Wood, Pat; Merrick, Lynda; Lincoln, D. W. Department of Anatomy, University of Bristol, Bristol, England **Opiate inhibition of peptide release from the neurohumoral terminals of hypothalamic neurones.** *Nature* 282(5740):746-748, 1979.

Evidence is presented that opiates inhibit the electrically-induced release of oxytocin by an action on or close to the axon terminals within the neurohypophysis. Observations that endogenous opioids tonically suppress the release of oxytocin in response to physiological stimuli are also reported. The data were obtained from experiments with lactating Wistar rats and indicate that opiates such as morphine or naloxone inhibit peptide release from the neurohumoral terminals of hypothalamic neurones. 23 references. (Author abstract modified)

001146 Cohen, Bruce M; Herschel, Michael; Aoba, Anri. Dept. of Psychiatry, Harvard Medical School, Cambridge, MA 02115 **Neuroleptic, antimuscarinic, and antiadrenergic activity of chlorpromazine, thioridazine, and their metabolites.** *Psychiatry Research* 1(2):199-208, 1979.

Radioreceptor assays were used on calf brains to determine the neuroleptic, antimuscarinic, and antialpha noradrenergic potency of chlorpromazine, thioridazine, and their metabolites. The results indicate that these metabolites show a wide range of potencies. The spectrum of activity of a metabolite may be quite different from that of its parent compound. The clinical relevance of these findings to individual differences in drug response is discussed, and the combined use of radioreceptor assays and chemical assays in future clinical research is proposed. 23 references. (Author abstract modified)

001147 Colburn, Wayne A.; Bekersky, Ihor; Min, Bo H.; Hodshon, Barbara J.; Garland, William A. Dept. of Pharmacokinetics and Biopharmaceutics, Hoffman-La Roche Inc., Nutley, NJ 07110 **Contribution of gut contents, intestinal wall and liver to the first-pass metabolism of clonazepam in the rat.** *Research Communications in Chemical Pathology and Pharmacology* 27(1):73-90, 1980.

The first pass metabolism of clonazepam by the gut contents, intestinal wall, and liver of the male Sprague-Dawley rat was studied, using pharmacokinetic techniques and a glass chromatographic, chemical ionization, mass spectrometric, double labeling method. After simultaneous oral and intravenous administration of isotopic variants of clonazepam, the absolute bioavailability was 7.2%. Gut contents, intestinal wall, and liver contributed 42.4%, 39.6%, and 10.8%, respectively, to the 92.8% overall first pass metabolism. Intestinal wall and liver clearance were both greater than hepatic blood flow, suggesting extensive first pass metabolism at each site. In situ experiments with proximal segments of rat intestine indicated that the gut contents and intestinal epithelium metabolized about 20% of the available clon-

azepam to its amino metabolite in 1 hour. 19 references. (Author abstract modified)

001148 Cole, Alison E.; Shinnick-Gallagher, Patricia. Dept. of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77550 **Alpha-adrenoceptor and dopamine receptor antagonists do not block the slow inhibitory postsynaptic potential in sympathetic ganglia.** *Brain Research* 187(1):226-230, 1980.

Experiments which demonstrate that the slow inhibitory postsynaptic potential (S-IPSP) in the rabbit superior cervical ganglion (RSCG) is not specifically blocked by catecholamine antagonists are described. To study the effects of dopamine antagonists on the S-IPSP response in RSCG, ganglia excised from adult male New Zealand white rabbits were superfused with increasing concentrations of sulpiride and haloperidol until all ganglionic potentials were depressed. Similar results were found with the alpha-adrenoceptor antagonists phentolamine and yohimbine. Only the muscarinic antagonist, atropine, inhibited the S-IPSP and the slow excitatory postsynaptic potential (S-EPSP) without depressing the (nicotinic) fast excitatory postsynaptic potential (F-EPSP). Results support the alternative hypothesis for the generation of the S-IPSP proposed by Volle and Weight, that acetylcholine directly hyperpolarizes sympathetic ganglia via muscarinic receptors. 26 references.

001149 Concannon, James T.; Riccio, David C.; McKelvey, James. Riccio: Dept. of Psychology, Kent State University, Kent, OH 44242 **Pavlovian conditioning of fear based upon hormonal mediation of prior aversive experience.** *Animal Learning and Behavior* 8(1):75-80, 1980.

Rats were tested to determine if epinephrine administered to Ss given prior shock might support learning to new environmental cues paired with the epinephrine injection. Using non-naive and naive rats, a dose dependent effect in this direction occurred although it did not appear to be based on either epinephrine-induced place aversion or sensitization. The potential contribution of generalized fear, impairment of extinction of fear, and nonspecific sensitization to the phenomenon was then examined. The findings do not support these alternative interpretations and it appears the epinephrine administration to previously stressed rats supports new learning. It is suggested that the epinephrine cue association may be mediated by either of two mechanisms, and the hormonal redintegrative function of epinephrine injections is discussed in terms of modulating memory processing. 18 references. (Author abstract modified)

001150 Consolo, Silvana; Ladinsky, Herbert; Tirelli, Amedea Silvia; Crunelli, Vincenzo; Samanin, Rosario; Garattini, Silvio. Istituto di Ricerche Farmacologiche Eritrea, 62, I-20157 Milan, Italy **Increase in rat striatal acetylcholine content by d-fenfluramine, a serotonin releaser.** *Life Sciences* 25(23):1975-1981, 1979.

The selective action of d-fenfluramine, a powerful releaser of serotonin (5-HT), in increasing acetylcholine (ACh) content was investigated. The anorectic agent, d-fenfluramine, was found to maximally increase the ACh content in the rat striatum by 50% at doses of 5 to 10mg/kg. The action of the drug was completely prevented by treatments designed to interfere with serotonergic transmission (e.g., combined electrolytic lesion of the nucleus raphe medianus and dorsalis; pretreatments with methergoline, parachlorophenylalanine, or fluoxetine). By contrast, interference with dopaminergic transmission did not impede the action of d-fenfluramine. The administration of d-fenfluramine to animals given a supramaximal dose of apomorphine, 1.5mg/kg, produced a summated increase in striatal acetylcholine. The data are consistent with the hypothesis that there may exist in the striatum different populations of cholinergic interneurons

regulated by serotonin and dopamine, respectively. 20 references. (Author abstract modified)

001151 Conway, E. L.; Louis, W. J.; Jarrott, B. University of Melbourne, Clinical Pharmacology and Therapeutics Unit, Austin Hospital, Heidelberg 3084, Victoria, Australia **The effect of acute alpha-methyl-dopa administration on catecholamine levels in anterior hypothalamic-preoptic and medullary nuclei in rat brain.** *Neuropharmacology*. 18(3):279-286, 1979.

Subcutaneous administration of 200mg/kg alpha-methyl-dopa to male Sprague-Dawley rats resulted in a marked reduction of noradrenaline and dopamine in anterior hypothalamic/preoptic nuclei implicated in catecholamine mediated cardiovascular inhibitory functions. Similar effects were observed in medullary nuclei, including the nucleus tractus solitarius. The metabolite alpha-methyl-dopamine accumulated rapidly. Four hours after drug administration, levels of alpha-methyl-dopamine were higher in most nuclei than in the medulla oblongata or hypothalamus as a whole, suggesting greater uptake of alpha-methyl-dopa into these specific areas. Levels of alpha-methylnoradrenaline were also higher in the nuclei than in the gross tissues. The time course of accumulation and disappearance of alpha-methylnoradrenaline in the nucleus tractus solitarius differed from that in the anterior hypothalamic/preoptic nuclei and more closely correlated with the reported time course of the hypotensive effect of alpha-methyl-dopa. 27 references. (Author abstract modified)

001152 Conway, E. L.; Louis, W. J.; Jarrott, B. University of Melbourne, Clinical Pharmacology and Therapeutics Unit, Austin Hospital, Heidelberg, 3084, Victoria, Australia **Endogenous and alpha-methylated catecholamine levels in anterior hypothalamic-preoptic and medullary nuclei in rat brain after chronic alpha-methyl-dopa administration.** *Neuropharmacology*. 18(3):287-290, 1979.

Chronic subcutaneous administration of alpha-methyl-dopa (40mg/kg, twice daily for 5 days) to male Sprague-Dawley rats produced a profound depletion of noradrenaline and dopamine levels in nuclei from the anterior hypothalamic region and medulla oblongata. Four hours after the last injection, noradrenaline and dopamine were virtually undetectable in these nuclei, whereas high levels of alpha-methylnoradrenaline and low levels of alpha-methyl-dopamine were detected in all nuclei. Amine levels began to recover 24 hours after the last injection of alpha-methyl-dopa, but alpha-methylnoradrenaline concentrations were still between 50 and 80% of 4 hour values and noradrenaline levels were still less than 45% of control values. These findings suggest that alpha-methylnoradrenaline is involved in mediating the hypotensive effect of alpha-methyl-dopa. The slow recovery of amine levels may explain the persistence of the hypotensive effect of this drug. 14 references. (Author abstract modified)

001153 Costa, Erminio; Cheney, Darwin L. Laboratory of Pre-clinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Functional interactions of neurotransmitter systems.** (Unpublished paper). Washington, DC, NIMH, 1979. 12 p.

Studies of the transmitter interactions in the septal nuclei in rats are summarized to illustrate the potential of the measurement of the turnover rates of neurotransmitters in various nuclei in the detection of functional interactions between neurotransmitter systems in a neuronal pathway. It is demonstrated that the turnover rate of acetylcholine located in the axon terminals of the hippocampus can be modulated as a result of transmitter interactions that are operative in the septum where the dendrites of the cholinergic neurons are located. It is also shown that the metabolic state of hippocampal acetylcholine can also be regu-

lated by the activity of the axo axonic synapses that control cholinergic nerve endings in the hippocampus. 61 references.

001154 Cote, Thomas; Munemura, Masahide; Keabian, John. Experimental Therapeutics Branch, NINCDS, Building 10, Room 6D16, NIH, Bethesda, MD 20205 **Lisuride hydrogen maleate: an ergoline with beta-adrenergic antagonist activity.** *European Journal of Pharmacology*. 59(3/4):303-306, 1979.

The potent beta-adrenergic antagonist properties of lisuride hydrogen maleate were demonstrated, using a hormone sensitive adenylate cyclase system and (3H)dihydroalprenolol binding in cell free homogenates of rabbit cerebellum. Lisuride and two other ergolines, lergotril and bromocriptine, interacted with spiroperidol binding sites in the anterior pituitary, as did the phenothiazine fluphenazine. Among these compounds, only lisuride antagonized the beta-adrenoceptor. 10 references. (Author abstract modified)

001155 Coupet, Joseph; Rauh, Charles E.; Szues-Myers, Vera A.; Yunger, Libby M. Dept. of Central Nervous System Research, Lederle Laboratories, Pearl River, NY 10965 **2-Chloro-11-(1-piperazinyl)dibenz(b,f) (1,4)oxazepine (Amoxapine), an antidepressant with antipsychotic properties -- a possible role for 7-hydroxyamoxapine.** *Biochemical Pharmacology*. 28(16):2514-2515, 1979.

Amoxapine and its hydroxylated metabolites, 7-hydroxyamoxapine (7-OH-Amox) and 8-hydroxyamoxapine (8-OH-Amox), were tested in vitro for effects indicative of potential antipsychotic or antidepressant action. Amoxapine and 7-OH-Amox were comparable to imipramine in inhibiting the uptake of tritiated norepinephrine into male Wistar rat brain synaptosomes, but had little effect on the uptake of labeled serotonin. Amoxapine was moderately active in displacing tritiated spiroperidol binding and inactive in preventing dopamine stimulation of adenylate cyclase, whereas 7-OH-Amox was strongly active in both assays. Results suggest a major role for 7-OH-Amox in mediating the antidopaminergic effects of amoxapine. 16 references. (Author abstract modified)

001156 Crabbe, John C.; Rigter, Henk. Research Service, Veterans Administration Medical Center, Portland, OR **Learning and the development of alcohol-tolerance and dependence: the role of vasopressin-like peptides.** *Trends in NeuroSciences*. 3(1):20-23, 1980.

The research literature on the role of vasopressin-like peptides in learning and the development of alcohol tolerance and dependence is reviewed. Although tolerance and physical dependence traditionally have been considered as early and late manifestations, respectively of the same or closely related physiological phenomena, recent research indicates that they appear to develop roughly in parallel. It is noted that there have been several adequate rodent models developed for the study of tolerance to and physical dependence on ethanol. Application of these models may greatly increase knowledge about the early stages of tolerance and dependence development. It is hypothesized that learning in the development of tolerance and dependence on alcohol (and opiates) represents a substrate of vasopeptide influences. Direct evidence for the involvement of learning in the development of tolerance and dependence is reviewed, and the role of vasopressin in memory, tolerance to, and dependence on alcohol is discussed. 18 references. (Author abstract modified)

001157 Crain, Stanley M.; Crain, Bea; Finnigan, Tara; Simon, Eric J. Dept. of Neuroscience, Albert Einstein College of Medicine, Bronx, NY 10461 **Development of tolerance to opiates and opioid peptides in organotypic cultures of mouse spinal cord.** *Life Science*. 25(21):1797-1802, 1979.

Following chronic exposure of organotypic explants of mouse spinal cord with attached dorsal root ganglia (DRG) to low levels (1mM) of morphine for 2 to 3 days at 35 degrees C, the initial opiate depressant effects on sensory evoked dorsal horn network responses disappeared. Characteristic dorsal cord responses could then be evoked by DRG stimuli in the presence of morphine, even after acute increases in concentration up to 100-fold. Similar tolerance was observed after chronic exposure of cord/DRG explants to low concentrations (10nM) of a synthetic enkephalin analogue. Cross-tolerance was observed between morphine, met-enkephalin, and the enkephalin analogue. Tolerance was not observed when cultures were incubated at a lower temperature (20 degrees) and exposed to 1mM morphine for as long as 7 days. Results indicate that a temperature dependent metabolic change occurs in these neurons after chronic exposure to morphine at 35 degrees, leading to a sustained decrease in sensitivity to opiate depressant effects. 19 references. (Author abstract modified)

001158 Craves, Frederick B.; Zalc, Boris; Leybin, Leonid, Baumann, Nicole; Loh, Horace H. Dept. of Pharmacology, University of California, San Francisco, CA 94143 **Antibodies to cerebroside sulfate inhibit the effects of morphine and beta-endorphin.** Science. 207(4426):75-76, 1980.

The influence of antibodies to cerebroside sulfate on the effects of morphine and beta-endorphin was investigated. Morphine and beta-endorphin inhibit the shaking response of pentobarbital anesthetized rats to ice water. Stereotactically guided administration of antibodies to cerebroside sulfate into the periaqueductal gray region, the most sensitive brain region in which to demonstrate inhibition of this response, antagonizes the effect of morphine and beta-endorphin. These results suggest that cerebroside sulfate may be an integral component of an opiate receptor in rat brain. 12 references. (Author abstract modified)

001159 Crawford, Robert A.; Gregory, Peter C.; Griffiths, Ian R. Dept. of Veterinary Surgery, University of Glasgow Veterinary Hospital, Bearsden, Glasgow G61 1QH, Scotland **The response of feline spinal pial arterioles to norepinephrine.** Journal of Neurosurgery. 52(1):60-63, 1980.

The effect of norepinephrine (NE) on the diameter of feline spinal pial arteries and arterioles was studied by applying the drug to the perivascular environment. Microapplication of NE to spinal pial arterioles produced a concentration related constriction of the vessels, with a maximal constriction of 28.8% at 0.005M. This reduction was prevented when the alpha-adrenergic blocker phentolamine was injected with the NE. Results indicate that there are alpha-adrenergic receptors on the smooth muscle of spinal pial arterioles. 16 references. (Author abstract modified)

001160 Crawley, J. N.; Maas, J. W.; Roth, R. H. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Evidence against specificity of electrical stimulation of the nucleus locus coeruleus in activating the sympathetic nervous system in the rat.** Brain Research. 183(2):301-311, 1980.

Four experimental approaches were utilized to test the specificity of the central nucleus locus coeruleus (LC) cell group in activating the sympathetic nervous system (SNS) in the electrical stimulation paradigm. Varying the stimulation current amplitude, varying the site of stimulating electrode placement, and electrolytic lesions of the LC yielded results consistent with the hypothesis that the site of SNS activation was within the anatomical region of the LC cell group. Neurochemical lesioning with intraventricular 6-hydroxydopamine, however, did not effectively block the plasma 3-methoxy-4-hydroxyphenethyleneglycol (MHPG) increase observed after

stimulation of the LC region. The possibility that nonnoradrenergic cells, fibers of passage, or terminals in the LC region of the midbrain may be responsible for SNS activation when the LC is electrically stimulated is discussed. These studies are pertinent to all studies of LC function which employ electrical stimulation of the LC nucleus, including investigations of the role of the LC in social behavior, intracranial self-stimulation, and blood pressure regulation. 36 references. (Author abstract modified)

001161 Crawley, Jacqueline; Marangos, Paul J. Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **Reduced number of benzodiazepine receptors following chronic administration of clonazepam.** (Unpublished paper). Bethesda, MD, NIMH, 1980. 5 p.

Data are presented to show that a significant change in benzodiazepine receptor sensitivity results after mice are administered clonazepam for 3 weeks, but this decrease in forebrain benzodiazepine receptor number does not occur in mice treated with chlordiazepoxide. Preliminary experiments with acute administration of a single high dose of clonazepam suggest that the presence of the drug in brain is not sufficient to induce receptor subsensitivity since no significant decrease in Bmax was observed in these experiments. These results support the hypothesis that induction of receptor subsensitivity with chronic benzodiazepine treatment is a function of the relative binding potency of the ligand administered. 7 references.

001162 Creese, Ian; Stewart, Kim; Snyder, Solomon H. Snyder: Dept. of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Species variations in dopamine receptor binding.** European Journal of Pharmacology. 60(1):55-66, 1979.

The dopamine receptor binding of tritiated spiroperidol, apomorphine, and 2-amino-6,7-dihydroxytetrahydronaphthalene was evaluated in corpus striatal membranes of calf, rat, and human brains. Substantial species differences were found in agonist and antagonist competition for receptor binding. In general, dopamine receptor antagonists were more potent in the rat, while agonists were more potent in the calf preparation. Molindone and metaclopramide showed the most pronounced species differences in competing for 3H-spiroperidol binding, being three to ten times more potent in rat and human than in calf. In human amygdala, 3H-spiroperidol appeared to label predominantly serotonin receptors. 31 references. (Author abstract modified)

001163 Crews, Fulton T.; Morita, Yutaka; McGivney, Anne; Siraganian, Reuben; Hirata, Fusao; Axelrod, Julius. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Involvement of phospholipid methylation and phospholipase activation in arachidonic acid and histamine release in rat leukemic basophils.** (Unpublished paper). Bethesda, MD, NIMH, 1980. 1p.

To examine the role of phospholipid methylation, phospholipase A2, and arachidonate metabolites on the release of both arachidonate, a prostaglandin precursor, and histamine from rat leukemic basophils, the effects of various inhibitors were tested on histamine secretion as well as arachidonate release and metabolism. It was found that 3-deaza-adenosine, a methyltransferase inhibitor, blocked both histamine and arachidonate release. Mepacrine, a phospholipase A2 inhibitor, also prevented both histamine release and arachidonate release. Arachidonate, which is released from phospholipids by phospholipases, was metabolized primarily to prostaglandin D2. Inhibition of prostaglandin synthesis by indomethacin had no effect on either histamine or arachidonate release. Eicosatetraenoic acid inhibited both histamine and arachidonate release, but the inhibition of histamine

release required two orders of magnitude higher concentrations than the inhibition of arachidonate metabolism. These results suggest that both phospholipid methylation and phospholipase activation are important components for arachidonate release as well as exocytotic histamine release. (Author abstract modified)

001164 Crutcher, Keith A.; Davis, James N. Neurology Research Laboratory, Veterans Administration Medical Center, Durham, NC Hippocampal alpha- and beta-adrenergic receptors: comparison of (3H)dihydroalprenolol and (3H)WB 4101 binding with noradrenergic innervation in the rat. *Brain Research*. 182(1):107-117, 1980.

The relation of alpha-adrenergic and beta-adrenergic receptors to the noradrenergic innervation of the male Sprague-Dawley rat hippocampal formation was studied with histo-fluorescent, biochemical, and radioligand binding methods. The dentate gyrus received a major portion of the innervation and contained twice the norepinephrine content of the hippocampal gyrus. The density of beta-adrenergic receptors, determined by tritiated dihydroalprenolol (3H-DHA) binding, was about equal in the two gyri, but alpha-adrenergic binding sites were more concentrated in the dentate gyrus. Direct microchemical measurements of 3H-DHA binding in stratum pyramidale and stratum radiatum showed that beta-adrenergic receptors were uniformly distributed in the hippocampal gyrus. Results suggest that some beta-adrenergic receptors are not associated with noradrenergic nerve terminals. 26 references. (Author abstract modified)

001165 Dafny, N.; Rigor, B. M.; Burks, T. F. University of Texas Medical School, Houston, TX 77025 Dependence and tolerance: multiunit recording from central gray, mesencephalic reticular formation, and medial thalamus in freely behaving rats. *Experimental Neurology*. 68(2):217-227, 1980.

Administration of various dosages of morphine produced different response patterns in simultaneous, multiunit recordings from the medial thalamus, central gray, and mesencephalic reticular formation of freely moving rats previously implanted stereotactically with permanent semimicroelectrodes. The responses induced by morphine exhibited dose related patterns, and could be reversed by naloxone. The optimal dose for all three brain structures was 10mg/kg morphine. This dose was used as a challenge dose in morphine dependent rats, which demonstrated electrophysiologic patterns of morphine physical dependence and tolerance. 22 references. (Author abstract)

001166 Dafny, Nachum. Dept. of Neurobiology and Anatomy, University of Texas Medical School, Houston, TX 77025 Two photic pathways contribute to pineal evoked responses. *Life Sciences*. 26(9):737-742, 1980.

The transmission of photic responses to the pineal via the superior cervical ganglion (sc)/nervi conorii and/or through the habenular posterior commissure complex were investigated via analysis of photically evoked responses in freely behaving rats. Average photic evoked responses were recorded simultaneously from the pineal body and the ventromedial hypothalamus via implanted semimicroelectrodes following local anesthesia (xylocaine), sympathectomy, and/or general anesthesia (barbiturate). Results indicate that the photic evoked responses recorded from the pineal are transmitted via two separate routes: one, a fast pathway with a shorter latency, via the CNS, i.e., the habenular posterior commissure complex, and the other, a slower (or longer) pathway via the scg to the pineal. 23 references. (Author abstract modified)

001167 Davies, Bruce; Abood, Leo; Tometsko, Andrew M. Dept. of Biochemistry, University of Rochester Medical Center,

Rochester, NY 14642 Utilization of 3H-dopamine as a photoaffinity label of brain synaptosomes. *Life Sciences*. 26(2):85-88, 1980.

The possibility of utilizing 3H-dopamine as a photoaffinity label for rat brain synaptosomes was investigated. It is noted that the 3H-dopamine interacts covalently with intact and disrupted synaptosomes in the absence of light, but the interaction increases as much as fourfold following flash photolysis with ultraviolet light. The photolytic interaction in intact, but not disrupted, synaptosomes is inhibited by benzotropine and cocaine, but not by haloperidol. It is concluded that a major photolytic reactive site in synaptosomes is that associated with dopamine reuptake. 7 references. (Author abstract)

001168 Davies, Les P.; Cook, Alan F.; Poonian, Mohindar; Taylor, Kenneth M. Roche Research Institute of Marine Pharmacology, P.O. Box 225, Dee Why, 2099 N.S.W. Australia Displacement of (3H) diazepam binding in rat brain by dipyridamole and by 1-methylisoguanosine, a marine natural product with muscle relaxant activity. *Life Sciences*. 26(13):1089-1095, 1980.

1-Methylisoguanosine, a marine natural product isolated from the sponge *Tedania digitata*, and a number of closely related synthetic analogues were tested for their ability to displace (3H) diazepam binding to rat brain membranes. Of all the purines yet tested, the natural product was the most active, being some tenfold better than 2-deoxyguanosine, the most potent purine so far reported in the literature. Other analogues in which only the ribose moiety was altered displayed very similar activity, whereas alteration of the 1-methylisoguanine base markedly reduced their ability to displace bound diazepam. The adenosine uptake blocker dipyridamole was shown to be relatively potent as a diazepam displacer. The need for in vivo studies of the analogues is noted. 15 references. (Author abstract modified)

001169 Davies, Les P.; Taylor, Kenneth M.; Gregson, Richard P.; Quinn, Ronald J. Roche Research Institute of Marine Pharmacology, P.O. Box 255, Dee Why, N.S.W. Australia Stimulation of guinea-pig brain adenylate cyclase by adenosine analogues with potent pharmacological activity in vivo. *Life Sciences*. 26(13):1079-1088, 1980.

The ability of the marine natural product, 1-methylisoguanosine, and a series of related synthetic analogues to activate the adenosine stimulated adenylate cyclase of guinea pig brain was examined to see whether this was related to the muscle relaxant and cardiovascular properties of a number of these compounds. The ability of some of these compounds to undergo deamination by adenosine deaminase and to share the same uptake system as adenosine was also examined. Compounds lacking the adenylate cyclase stimulating ability were found to have little muscle relaxant activity. Unlike adenosine, 1-methylisoguanosine was resistant to deamination and only poorly accumulated by brain tissue slices or homogenates containing synaptosomes. Since it is an extremely weak competitive inhibitor of adenosine deaminase and only a weak inhibitor of adenosine uptake, it is concluded that it is unlikely to act by potentiating the effects of adenosine itself at extracellular receptors. It is suggested that the pharmacological effects of 1-methylisoguanosine are due to its actions as a long lasting adenosine analogue. 76 references. (Author abstract modified)

001170 De Catanzaro, Denys; Gorzalka, Boris B. Dept. of Psychology, McMaster University, Hamilton, Ontario, Canada L8S 4K1 Effects of dexamethasone, corticosterone, and ACTH on lordosis in ovariectomized and adrenalectomized-ovariectomized rats. *Pharmacology Biochemistry and Behavior*. 12(2):201-206, 1980.

The involvement of the pituitary adrenocortical axis in the control of the lordosis reflex was investigated. In the first experiment, estrogen primed ovariectomized (ovx) and adrenalect-

tomized/ovariectomized (adx/ovx) females were treated chronically with dexamethasone, a compound blocking ACTH release from the pituitary. Dexamethasone inhibited lordosis, effectively blocking an adrenalectomy-induced facilitation of the reflex. In the sec. experiment, corticosterone was similarly administered chronically; this compound also inhibited lordosis in adx/ovx females. In experiment 3, acute peripheral administration of synthetic ACTH caused a marked increase in lordosis in ovx females. The results suggest that in the adrenalectomized animal, ACTH may exert its effect through adrenal steroids. An acute elevation of adrenal steroids may increase lordosis, whereas a chronic elevation may decrease it. 23 references. (Author abstract)

001171 de Cotte, D. Marcano; De Menezes, C. E. L.; Bennett, G. W.; Edwardson, J. A. Edwardson: Medical Research Council Neuroendocrinology Unit, Newcastle General Hospital, Westgate Road, Newcastle upon Tyne, England **Dopamine stimulates the degradation of gonadotropin releasing hormone by rat synaptosomes**. *Nature*. 283(5746):487-489, 1980.

The effects of dopamine on the degradation of gonadotropin releasing hormone (LH/RH) by rat synaptosomes were investigated. In nerve endings isolated from the rat hypothalamus, higher doses of dopamine stimulated the degradation of LH/RH but not thyrotropin releasing hormone (TRH). This mechanism seems to be physiological in that it is calcium dependent, requires the structural integrity of the nerve endings and fluctuates with the reproductive state of the animal. It is suggested that dopamine not only regulates the release of LH/RH, but actually regulates the disposal of this hormone by controlling peptidase activity at the nerve terminal. 18 references. (Author abstract modified)

001172 De Langen, Cees D. J.; Hogenboom, Francois; Mulder, Arie H. Mulder: Dept. of Pharmacology, Free University Medical Faculty, Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands **Presynaptic noradrenergic alpha-receptors and modulation of 3H-noradrenaline release from rat brain synaptosomes**. *European Journal of Pharmacology*. 60(1):79-89, 1979.

The effects of alpha-noradrenergic drugs on the depolarization (15mM potassium) induced release of tritiated noradrenaline (NA) from superfused male Wistar rat brain synaptosomes were studied. In the presence of the uptake inhibitor desipramine, NA reduced synaptosomal release of 3H-NA, and this effect was enhanced when the concentration of calcium ions in the medium during potassium stimulation was reduced. Under these conditions, NA produced a dose dependent inhibition of 3H-NA release from synaptosomes obtained from the cortex or hypothalamus, but not from striatal synaptosomes. Adrenaline, clonidine, and oxymetazoline potentially inhibited 3H-NA release from cortex synaptosomes. Phentolamine did not itself affect synaptosomal 3H-NA release, but antagonized the inhibitory effects of NA and adrenaline. Results support the hypothesis that the alpha-receptors mediating local negative feedback control of NA release are located on the varicosities of central noradrenergic neurons. 19 references. (Author abstract modified)

001173 de Langen, Cees D. J.; Stoof, Johannes C.; Mulder, Arie H. Mulder: Dept. of Pharmacology, Free University, Medical Faculty, Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands **Studies on the nature of the releasable pool of dopamine in synaptosomes from rat corpus striatum: depolarization-induced release of 3H-dopamine from superfused synaptosomes labelled under various conditions**. *Naunyn-Schmiedeberg's Archives of Pharmacology*. 308(1):41-49, 1979.

The accumulation and postassium evoked release of tritiated dopamine (3H-DA) from male Wistar rat corpus striatum synap-

tosomal preparations superfused with 3H-DA were quantified. The percentage of 3H-DA released and the distribution of 3H-DA into intrasynaptosomal transmitter pools were independent of the amount of 3H-DA accumulated in the synaptosomes. The release of 3H-DA was depressed upon repeated depolarization, probably as a result of selective depletion of a releasable pool rather than an impairment of stimulus/secretion coupling processes. When synaptosomes were subjected twice to potassium stimulation and exposed to 3H-DA before the first stimulation or between the two stimulations, the most recently accumulated 3H-DA was released in preference to that previously accumulated. The 14C-DA synthesized in the synaptosomes from 14C-tyrosine was not released in preference to 3H-DA that entered the synaptosomal pools through the high affinity uptake mechanism. Results support the view that DA is stored heterogeneously in varicosities of nigrostriatal neurons in the rat. The slow redistribution of stored 3H-DA into synaptosomal pools indicated that differences in vesicle localization with respect to the nerve terminal membrane may explain the occurrence of different DA pools. 23 references. (Author abstract modified)

001174 Deadwyler, Sam A.; Robinson, John H. Dept. of Physiology and Pharmacology, Bowman Gray School of Medicine, Winston-Salem, NC 27103 **Effects of morphine on hippocampal cells recorded in vitro**. *Brain Research Bulletin*. 4(5):609-613, 1979.

Intracellular recordings from CA1 pyramidal cells in male Sprague-Dawley rat hippocampal slices were obtained before and after application of morphine sulfate. Within 3 to 10 minutes of morphine application, CA1 cell membrane potentials began to depolarize toward firing threshold. Spontaneous discharge rates were increased, and inactive cells became active. Rhythmic firing at a rate of 5 to 8Hz was observed for 30 to 40 minutes after drug application. The spontaneous firing rhythm could be partially reversed by addition of 0.1mM naloxone to the bathing media. Morphine also potentiated the development of epileptiform discharges in CA1 cells in response to low frequency orthodromic synaptic stimulation. Results indicate that morphine alters the excitability of hippocampal pyramidal cells, probably via opiate specific alterations in membrane conductance and/or tonic inhibitory synaptic inputs. 27 references. (Author abstract modified)

001175 DeFeudis, Francis V.; Ossola, Lucienne; Schmitt, Gaby; Mandel, Paul. Centre de Neurochimie du CNRS, Faculté de Médecine, F-67085 Strasbourg Cedex, France **Substrate specificity of (3H)muscimol binding to a particulate fraction of a neuron-enriched culture of embryonic rat brain**. *Journal of Neurochemistry*. 34(4):845-849, 1980.

The effects of some GABA analogues and some drugs on the binding of (3H)muscimol to thoroughly washed subcellular particles prepared from a neuron enriched culture of embryonic rat brain were examined. (3H)muscimol binding was potently inhibited by muscimol itself, GABA, isoguvacine, and 3-aminopropanesulphonic acid, and less potently inhibited by the GABA antagonist bicuculline methobromide. Delta-aminovaleric acid, the glycine/beta-alanine antagonist strychnine, and the predominantly glial GABA uptake inhibitors beta-alanine and beta-proline also inhibited (3H)muscimol binding. Other inhibitors of sodium dependent GABA uptake, nipecotic acid, L-2,4-diaminobutyric acid, and guvacine, as well as picrotoxinin, were relatively inactive as inhibitors of (3H)muscimol that occurs to neuronal, but not to glial, membranes might be useful as a neuronal marker and for the further characterization and isolation of GABA receptors. 33 references. (Author abstract modified)

001176 DeFrance, Jon; Stanley, James; Marchand, James; Enna, Salvatore J. Enna: University of Texas Medical School, P.O. Box 20708, Houston, TX 77025 **The effect of muscimol on hippocampal pyramidal cells.** *European Journal of Pharmacology.* 59(1/2):155-158, 1979.

The effects of muscimol on the firing of hippocampal pyramidal cells were examined in male New Zealand rabbits. When administered iontophoretically, topically, or intravenously, muscimol produced a bicuculline sensitive, strychnine insensitive depression of the monosynaptically activated population spike evoked by microstimulation of the contralateral hippocampal field. Results indicate that systemically administered muscimol selectively activates hippocampal GABA receptors and may be useful for studying limbic system physiology. 10 references. (Author abstract modified)

001177 Della Corte, Laura; Tipton, Keith F. Instituto Interfacoltà di Farmacologia e Tossicologia, Università di Firenze, Viale G. B. Morgagni 65, I-50134 Firenze, Italy **The turnover of the A- and B-forms of monoamine oxidase in rat liver.** *Biochemical Pharmacology.* 29(6):891-895, 1980.

The inhibition of rat liver monoamine oxidase was determined following the intraperitoneal injection of the inhibitors clorgyline and pargyline in order to establish the concentration ranges in which substrate selective inhibition occurred. The rate of recovery of the activity of the A-form of the enzyme after inhibition by clorgyline was determined using tyramine and serotonin as substrates, and the rate of recovery of the activity of the B-form after inhibition by pargyline was determined using tyramine and 2-phenylethylamine as substrates. No significant differences could be detected between the rates of recoveries of the two forms which corresponded to a rate constant for degradation of the enzyme of about 0.27 day. Results are compared with those of previous studies on enzyme activity in other organs. 36 references. (Author abstract modified)

001178 Della-Fera, Mary Anne; Baile, Clifton A. School of Veterinary Medicine, University of Pennsylvania, Kennett Square, PA 19348 **Cholecystokinin octapeptide: continuous picomole injections into the cerebral ventricles of sheep suppress feeding.** *Science.* 206(4417):471-473, 1979.

The effect of the cholecystokinin octapeptide (CCK) on feeding behavior of sheep was examined. CCK decreased food intake in a dose related manner when injected continuously into the lateral cerebral ventricles of sheep that had been deprived of food for 2, 4, 8, or 24 hours. In sheep deprived of food for 2 hours, as little as 0.01 picomole min suppressed feeding by 35% 1 hour after beginning injection. Pentagastrin also decreased feeding in the 2 hour group, but only at a much higher dose range. Secretin had no effect. Findings support the hypothesis that CCK acts on CNS structures involved in control of food intake. 16 references. (Author abstract modified)

001179 Dennis, Stephen G.; Melzack, Ronald; Gutman, Samuel; Boucher, Francoise. Melzack: Dept. of Psychology, McGill University, 1205 Avenue Docteur Penfield, Montreal, Quebec, Canada H3A 1B1 **Pain modulation by adrenergic agents and morphine as measured by three pain tests.** *Life Sciences.* 26(15):1247-1259, 1980.

The effects of several adrenergic agents on pain and morphine analgesia were assessed using three pain tests in rats: tail/flick, hotplate, and formalin. Each pain test yielded a unique constellation of adrenergic influences, suggesting that variation of stimulus and response parameters can change the functional expression of adrenergic systems related to pain processing. The salient drug effects include a pronounced, relatively selective analgesic effect of yohimbine in the hotplate test; a selective an-

algesic effect of clonidine in the formalin test; a striking but variable antagonism of morphine analgesia by a combination of yohimbine and propranolol in the formalin test; a nonlinear dose/response curve for antagonism of morphine analgesia by propranolol in the hotplate test; and a generalized interference with pain responding and enhancement of morphine analgesia by most drugs in the formalin test. Data suggest that the type of pain test is crucial in determining the pattern of drug influences that is revealed. 39 references. (Author abstract modified)

001180 Desclin, J. C.; Colin, F. Laboratoire d'Histologie, Faculté de Médecine, Université Libre de Bruxelles, Brussels, Belgium **The olivocerebellar system. II. Some ultrastructural correlates of inferior olive destruction in the rat.** *Brain Research.* 187(1):29-46, 1980.

Short-term and long-term ultrastructural changes induced in rat inferior olivary nucleus (ION) and cerebellum by a single injection of 3-acetylpyridine (3-AP) were investigated. Evidence of perikaryal and dendritic alterations was already present in numerous ION neurons at 3 hours after injection. All ION neurons were affected at 6 hours. Complete destruction of the entire ION was achieved within 8 to 10 hours. Time course and cytological features of this degeneration were described. Total absence of axonal terminal degeneration in the ION or at its periphery ruled out the existence of recurrent olivary axons in these locations. Climbing fiber (CF) terminal degeneration in the cerebellar cortex apparently was restricted to the molecular layer, which cast serious doubts on the existence of glomerular collaterals of CFs. Evidence of axonal terminal degeneration was observed within all cerebellar nuclei at 24 hours and 26 hours after 3-AP treatment, but degenerating profiles were unexpectedly infrequent. Consequential to CF deafferentation, Purkinje cells underwent both precocious and delayed ultrastructural changes. Delayed and long-range changes involved mainly dendrites and perikarya. Axon terminals underwent precocious but prolonged alterations which were interpreted as evidence supporting enhanced synaptic activity of Purkinje cells deprived of CFs. 53 references. (Author abstract)

001181 Dewhurst, W. G.; McKim, H. R. Dept. of Psychiatry, 1st Floor, Clinical Sciences Building, University of Alberta, Edmonton, Alta. T6G 2G3, Canada **Pharmacological effects of p-chloroamphetamine with respect to current amine hypotheses of affective disorders.** *Neuropsychobiology.* 6(2):66-71, 1980.

The effects of p-chloroamphetamine (pCA) on the regional distribution of dopamine, noradrenaline, and 5-hydroxytryptamine in rat brain were studied. It was found that pCA has no significant effect on the levels of dopamine or noradrenaline. Conversely, pCA had an effect on the levels of 5-hydroxytryptamine but the effect was both time and area dependent. As an antidepressant, pCA has been shown to be effective. Since the levels of 5-hydroxytryptamine were reduced in all areas studied and there was no effect on the levels of the two catecholamines, the results do not support an amine hypothesis in which these transmitters are implicated. 26 references. (Author abstract)

001182 Dhalla, Naranjan S.; Lee, Sheu L.; Takeo, Satoshi; Panagia, Vincenzo; Bhayana, Veena. Division of Experimental Cardiology, Dept. of Physiology, Faculty of Medicine, University of Manitoba, Winnipeg, Canada R3E 0W3 **Effects of chlorpromazine and imipramine on rat heart subcellular membranes.** *Biochemical Pharmacology.* 29(4):629-633, 1980.

The effects of chlorpromazine and imipramine at concentrations ranging from 25 to 120mM on ATPase activities, as well as calcium binding and uptake abilities of the rat heart subcellular membranes, were studied in vitro. Chlorpromazine significantly decreased calcium binding Mg2ATPase and NaKATPase

activities of the sarcolemmal fraction, whereas imipramine decreased calcium binding, Ca²⁺ATPase and Mg²⁺ ATPase activities. Chlorpromazine also produced significant inhibition of the calcium binding and uptake abilities of the microsomal and mitochondrial fractions, while imipramine depressed the mitochondrial calcium uptake activity only at concentrations of 80mM or higher. The mitochondrial respiratory and oxidative phosphorylation activities were depressed at high concentrations of these drugs. Since different membrane systems have been considered to be involved in the regulation of heart function and metabolism, the observed decreases in ATPase and calcium accumulating activities of the heart subcellular membranes may represent one of the molecular mechanisms for the cardio-depressant actions of chlorpromazine and imipramine. 33 references. (Author abstract)

001183 Di Chiara, G.; Porceddu, M. L.; Morelli, M.; Mulas, M. L.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Evidence for a GABAergic projection from the substantia nigra to the ventromedial thalamus and to the superior colliculus of the rat.** *Brain Research.* 176(2):273-284, 1979.

Unilateral intranigral infusion of kainic acid (1.5mcg) in male Sprague-Dawley rats produced neuronal loss in the lateral two thirds of the nigra, but spared axons en passage. Fink-Heimer silver impregnation revealed dense terminal degeneration in the nigra and in areas of nondopaminergic nigral projection, such as the ventromedial (VM) nucleus of the thalamus, superior colliculus, and reticular formation; only sparse terminal degeneration was found in the caudate and septum. Seven days after the kainic acid lesion, glutamic acid decarboxylase activity was reduced significantly in the VM (33%), superior colliculus (40%), and substantia nigra (18%), but not in the ventrobasal thalamic nucleus of the lesioned side. Choline acetyltransferase was not altered in these areas. These findings suggest the existence of a nigrothalamic and nigrocollicular GABA mediated pathway, which may play an important role in motor coordination and gaze control. 34 references. (Author abstract modified)

001184 Di Giorgia, R. M.; Macaione, S.; Lanotte, M.; Nistico, G. Institute of Biochemistry, Faculty of Medicine, University of Messina, Messina, Italy **Effects of L-dopa on GABA metabolism in chick brain and retina.** *Neuropharmacology.* 18(10):777-781, 1979.

The effects of subacute oral treatment with L-dopa (125 or 250mg/kg/day for 8 days) on glutamic acid decarboxylase (GAD), GABA, and GABA transaminase (GABA-T) activities were determined in chick nucleus basalis, brain hemispheres, brainstem, and retina. In the nucleus basalis, which is homologous to the mammalian striatum, a significant increase in GAD activity was found, along with an increase in GABA content and a decrease in GABA-T activity. Similar effects were observed in brainstem, except that GABA-T was stimulated. In brain hemispheres, L-dopa decreased GAD and GABA-T activity. In retina, GABA content was increased and GABA-T activity significantly decreased, but GAD activity was unchanged. Results indicate that L-dopa can alter GABA turnover in some portions of the brain. 44 references. (Author abstract modified)

001185 Dichter, Marc A. Dept. of Neurology Children's Hospital Medical Center, 300 Longwood Ave, Boston, MA 02115 **Physiological identification of GABA as the inhibitory transmitter for mammalian cortical neurons in cell culture.** *Brain Research.* 190(1):111-121, 1980.

Rat cortical neurons were studied between 3 and 7 weeks in vitro to develop physiological data which demonstrate a transmitter role for GABA. Rat cortical neurons grown in dissociated cell culture exhibit IPSPs which appear to be generated by

an increase in membrane conductance to chloride. The neurons are all sensitive to GABA in micromolar concentrations and GABA mimics the inhibitory transmitter. The neurons are much less sensitive to glycine and insensitive to taurine. Bicuculline and strychnine both block essentially all IPSPs and at the same concentrations block GABA effects. It is concluded that GABA is in the main, or only, inhibitory transmitter utilized by the cortical neurons in vitro. The relevance of this conclusion to in situ transmitter identification is discussed. 31 references. (Author abstract modified)

001186 Dodson, R. A.; Johnson, W. E. College of Pharmacy, Idaho State University, Pocatello, ID 83209 **Effects of ethanol, arecoline, atropine and nicotine, alone and in various combinations, on rat cerebellar cyclic guanosine 3',5'-monophosphate.** *Neuropharmacology.* 18(11):871-876, 1979.

Cerebellar cyclic GMP concentrations were determined by radioimmune methods after sacrifice with focused microwave irradiation of male Sprague-Dawley rats pretreated with ethanol, arecoline, atropine, and nicotine. Arecoline and nicotine produced large increases in cerebellar cyclic GMP, but did not antagonize the depressive effects of ethanol. Atropine did not augment ethanol-induced decreases in cyclic GMP content. Results suggest that the depressant actions of ethanol on cerebellar cyclic GMP are independent of cholinergic mechanisms. 16 references. (Author abstract modified)

001187 Donzanti, Bruce A.; Warwick, Robert O. Warwick: Pharmacology Section, Dept. of Biological Sciences, Philadelphia College of Pharmacy and Science, Philadelphia, PA 19104 **Effect of methadone and morphine on serotonin uptake in rat periaqueductal gray slices.** *European Journal of Pharmacology.* 59(1/2):107-110, 1979.

The effects of d,l-methadone and morphine of tritiated serotonin (3H-5-HT) uptake were examined in slices of male Sprague-Dawley rat periaqueductal gray, a brain region quite sensitive to the analgesic effects of morphine. Methadone had a significant inhibitory effect on 3H-5-HT uptake, but morphine did not. The effects of methadone were significantly enhanced by naloxone. Systemic administration of methadone did not alter 3H-5-HT uptake. Results suggest that narcotic-induced blockade of 5-HT uptake mechanisms does not play a significant role in the expression of narcotic analgesia. 11 references. (Author abstract modified)

001188 Drew, Roger; Siddik, Zahid H. Dept. of Clinical Pharmacology, Flinders University of South Australia, Bedford Park, South Australia 5042 **Effect of a specific 5HT uptake inhibitor (citalopram) on drug accumulation by rat lung slices.** *Pharmacology.* 20(1):27-31, 1980.

Rat lung slices were used to examine the effects of citalopram, a compound reported to be a specific inhibitor of neuronal uptake of 5-hydroxytryptamine (5HT), on the pulmonary accumulation of 5HT, noradrenaline (NA), imipramine (IP), and paraquat (PQ). Citalopram inhibited 5HT uptake by 30% to 40% but NA uptake was not affected at any of the concentrations of citalopram studied. At the highest concentrations of citalopram (0.0001 to 0.0001 M/l) the accumulation of IP and PQ was reduced by 25% to 30%. It is concluded that at low concentrations, citalopram is a specific and potent inhibitor of 5HT uptake by rat lung slices. 18 references. (Author abstract modified)

001189 Drew, Roger; Sikic, Branimir I.; Mimnaugh, Edward G.; Litterst, Charles L.; Gram, Theodore E. Gram: Laboratory of Toxicology, NCI, NIH, Bethesda, MD 20205 **The distribution of 14C-imipramine in mice bearing Lewis lung carcinoma.** *Life Sciences.* 25(21):1813-1820, 1979.

The distribution of 14C-imipramine (10mg/kg i.p.) and several of its metabolites in tumor, lung, liver, and kidney was investigated in male BDF1 mice bearing Lewis lung carcinoma. In contrast to the other tissues, the tumor exhibited a pronounced absorption phase of 14C-imipramine: peak concentrations were reached about 2 hours after administration. The lung accumulated more imipramine than other tissues at early time points, but by 12 hours the lung had the lowest tissue/plasma ratio of 14C-imipramine derived radioactivity. The metabolic profile of imipramine was similar in lung and liver, with unchanged imipramine predominating; 2-hydroxyimipramine was the principal metabolite in liver. The presence of Lewis lung tumor had minimal effects on the distribution and metabolism of imipramine. 12 references. (Author abstract modified)

001190 Dubicka, Irene. State University of New York at Albany **The psychopharmacology of L-tryptophan: potentiation of tonic immobility duration in rabbits. (Ph.D. dissertation).** Dissertation Abstracts International. 40(2):969-B, 1979. Ann Arbor, Univ. Microfilms No. 7918778, 78p., 1979.

The psychopharmacology of the enhancement of tonic immobility by L-tryptophan (a serotonergic precursor) was investigated in the rabbit. The prolongation of tonic immobility by tryptophan was shown to peak at 45 minutes following either systemic injection or cerebroventricular microinfusion. Benserazide, a centrally acting decarboxylase inhibitor, completely blocked the tryptophan-induced potentiation of tonic immobility. Results support the serotonergic model of tonic immobility, and suggest that the potentiation by tryptophan is temporally associated with a localized serotonin increase in the midbrain raphe area. (Journal abstract modified)

001191 Dudai, Yadin; Yavin, Ziva; Yavin, Ephraim. Dept. of Neurobiology, Weizmann Institute of Science, Rehovot, Israel **Binding of (3H)flunitrazepam to differentiating rat cerebral cells in culture.** Brain Research. 177(2):418-422, 1979.

The ontogeny of benzodiazepine binding sites was examined in cultures of cells derived from fetal rat brain at 16 days gestation. Studies of the specific binding of tritiated flunitrazepam (3H-FNZ) indicated that the pharmacological properties of these sites were similar in immature and mature mammalian brain. Specific 3H-FNZ binding sites were already detectable in brain at 16 days gestation. Binding levels in the range of 0.2 and 0.4pmol/mg protein were observed in cultures of 1 to 13 days in vitro, and values up to 0.8pmol/mg protein were observed in homogenates of cultures maintained in vitro for 4 weeks. The level of 3H-FNZ binding sites in neuronal enriched cultures was similar to that in glial enriched cultures of the same age, suggesting that benzodiazepine binding sites are associated with both types of cells. 17 references.

001192 Duka, Theodora; Holtt, Volker; Herz, Albert. Dept. of Neuropharmacology, Max-Planck-Institut für Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany **In vivo receptor occupation by benzodiazepines and correlation with the pharmacological effect.** Brain Research. 179(1):147-156, 1979.

In an in vivo study of benzodiazepine receptor binding, the concentration of (3H)flunitrazepam in brain was monitored following i.v. injection of tracer doses into male NMRI mice. The accumulation of (3H)flunitrazepam 20 minutes after injection was highest in the hippocampus, cortex, and hypothalamus; intermediate in the striatum, medulla oblongata/pons, and midbrain; and lowest in the cerebellum. This corresponds well with the densities of benzodiazepine receptors found in vitro with the exception of medulla oblongata/pons and cerebellum. When increasing doses (0.01 to 10mg/kg) of unlabelled benzodiazepine derivatives (including flunitrazepam, clonazepam, and chlor-

diazepoxide) were injected simultaneously with (3H)flunitrazepam, a dose dependent, saturable, and stereospecific decrease of (3H)flunitrazepam, concentration in the mouse hippocampus was observed. The dose range in which the unlabeled benzodiazepines decreased (3H)flunitrazepam binding in hippocampus corresponds to that which inhibits pentylenetetrazol or picrotoxin-induced seizures, indicating that this in vivo method determines the occupation of pharmacologically relevant receptors. 18 references. (Author abstract modified)

001193 Duka, Theodora; Wuster, Michael; Herz, Albert. Dept. of Neuropharmacology, Max-Planck-Institut für Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany **Benzodiazepines modulate striatal enkephalin levels via a GABAergic mechanism.** Life Sciences. 26(10):771-776, 1980.

The hypothesized GABAergic mechanisms in the modulation of striatal enkephalin levels by benzodiazepines was investigated in rats. As measured by a highly specific radioimmunoassay, diazepam treatment of rats results in a rapid decrease of enkephalin levels in the striatum while these are increased in the hypothalamus. This striatal effect is mimicked by the GABA agonist muscimol and the GABA-transaminase inhibitor aminooxyacetic acid (AOAA). It is further blocked by the GABA antagonist bicuculline and is thus GABAergic in nature. Further, the diazepam effect upon striatal enkephalin levels is antagonized by low doses of naloxone. In the hypothalamus, diazepam effects were neither mimicked nor modulated by any of a variety of agonists and antagonists tested, suggesting that benzodiazepine effects on enkephalin levels in this structure are not mediated via a GABAergic mechanism. 18 references. (Author abstract modified)

001194 Dum, Jane; Meyer, Gabriele; Holtt, Volker; Herz, Albert. Dept. of Neuropharmacology, Max-Planck-Institut für Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany **In vivo opiate binding unchanged in tolerant/dependent mice.** European Journal of Pharmacology. 58(4):453-460, 1979.

The receptor binding of tritiated etorphine and naloxone was examined in vivo in the brains of naive NMRI mice and of mice made tolerant to and dependent on opiates by morphine pretreatment. Significant differences in the receptor binding of the opiate agonist and antagonist were found between naive and tolerant/dependent animals, but these differences disappeared 8 hours after interruption of the morphine supply, even though tolerance did not decline. Results suggest that morphine tolerance is a time dependent phenomenon not directly dependent on receptor occupation. 23 references. (Author abstract modified)

001195 Dunwiddie, T.; Mueller, A.; Palmer, M.; Stewart, J.; Hoffer, B. Hoffer. Dept. of Pharmacology, Box C236, University of Colorado Medical Center, 4200 E. Ninth Ave., Denver, CO 80262 **Electrophysiological interactions of enkephalins with neuronal circuitry in the rat hippocampus. I. Effects on pyramidal cell activity.** Brain Research. 184(2):311-330, 1980.

Effects of enkephalins on hippocampal pyramidal cell activity were studied in rats in situ and in the in vitro hippocampal slice. Active enkephalin derivatives produced a dose dependent naloxone reversible excitation in both preparations whereas inactive enkephalin derivatives had no effect. Several different types of experiments, carried out in the slice, strongly suggest that this excitation is due to blockage of inhibitory pathways. First, when the pyramidal cell population spike is increased during enkephalin administration, no change is seen in the simultaneously recorded EPSP. Second, the magnitude of the enkephalin effect is highly correlated with the amount of inhibition, as judged by paired pulse stimulation, initially present in the slice. Third, if inhibitory pathways are depressed by a brief period of hypoxia, enkephalin has little effect. Finally, enkephalin responses are

mimicked by picrotoxin, which selectively antagonizes inhibitory input to the pyramidal neuron. Since enkephalins do not block the effects of GABA, the putative inhibitory transmitter, these data suggest that opioid peptides depress the inhibitory interneurons and disinhibit the pyramidal cells. 85 references. (Author abstract)

001196 Dwoskin, L. P.; Sprague, G. L.; Takemori, A. E.; Sparber, S. B. Sparber: Dept. of Pharmacology, 105 Millard Hall, 435 Delaware Street, SE, University of Minnesota, Minneapolis, MN 55455 **Morphine release and displacement by naloxone in vivo in morphine naive and withdrawn rats.** *Life Sciences*. 26(5):377-385, 1980.

Morphine release and displacement by naloxone in vivo in morphine naive and withdrawn rats was investigated. Male Long-Evans rats, implanted in the lateral cerebroventricle with chronic indwelling push pull cannulae, were perfused for 120 minutes: 20 minutes with morphine in saline containing CaCl₂ vehicle, 40 minutes with vehicle, 20 minutes with morphine, 10 minutes with vehicle, and 30 minutes with naloxone in vehicle. These rats and drug naive rats were implanted s.c. with morphine pellets. After 72 hours the pellets were removed and 18 to 24 hours later the above perfusion procedure was repeated. The amount of morphine collected in the perfusate during the washout with naloxone was elevated, compared to the amount collected during the corresponding time of the washout with vehicle for both naive and withdrawn groups. The enhanced morphine release during the washout with naloxone did not differ significantly between the naive and withdrawn rats. However, significantly less morphine was recovered in the perfusate collected during the vehicle washout from the withdrawn rats, compared to that collected from the naive rats. Data suggest that in vivo morphine is specifically bound to receptors and is sensitive to naloxone displacement. It is also concluded that morphine is differentially taken up or otherwise disposed of by brains of rats which are in opiate withdrawal. 17 references. (Author abstract modified)

001197 Dyck, Lillian E.; Boulton, Alan A. Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan, Canada S7N 0X0 **The effect of reserpine and various monoamine oxidase inhibitors on the uptake and release of tritiated meta-tyramine, para-tyramine and dopamine in rat striatal slices.** *Research Communications in Psychology, Psychiatry and Behavior*. 5(1):61-78, 1980.

The monoamine oxidase (MAO) activity of rat striatal homogenates towards tritiated meta-tyramine (m-TA), para-tyramine (p-TA), and dopamine (DA) using conditions employed in uptake experiments was assayed. Such homogenates deaminated m-TA and p-TA faster than DA. Nialamide, iproniazid, pargyline, clorgyline, catron and parnate were able to inhibit striatal MAO activity in the order listed. The influence of these MAO inhibitors on the uptake of the tritiated amines into slices of the striatum was studied. Catron and parnate significantly reduced the uptake of all three amines, and therefore were not considered suitable for use in further uptake experiments. Pargyline and clorgyline offered good inhibition of MAO and did not inhibit uptake. 23 references. (Author abstract modified)

001198 Ebadi, M.; Kiangkalya, B. Dept. of Pharmacology, University of Nebraska College of Medicine, 42nd St. and Dewey Ave., Omaha, NB 68105 **On the mechanism of pyridoxal phosphate-related convulsions as implicated in enhanced transport of GABA.** *Neuropharmacology*. 18(3):301-307, 1979.

The effect of vitamin B6 (pyridoxine) on the uptake of GABA in male Sprague-Dawley rat synaptosomes was examined. The uptake of GABA into synaptosomes isolated from the

cerebral cortex of hippocampus was not altered by the B6 vitamers, pyridoxal, pyridoxamine, pyridoxal phosphate, or pyridoxamine phosphate; the vitamin B6 antimetabolite deoxypyridoxine; or the vitamin B6 depletors cycloserine or isoniazid. However, pyridoxal and pyridoxal phosphate enhanced GABA uptake in nuclear free crude homogenates of the cortex. These results do not support a direct involvement of vitamin B6 derivatives in the transport of GABA. The mechanism involved in pyridoxal phosphate related convulsions is discussed. 64 references. (Author abstract modified)

001199 Ebstein, Richard P.; Pickholz, Dalia; Belmaker, Robert H. Jerusalem Mental Health Center, Ezrath Nashim, POB 140, Jerusalem, Israel **Dopamine receptor changes after long-term haloperidol treatment in rats.** *Journal of Pharmacy and Pharmacology*. 31(8):558-559, 1979.

The kinetics of labelled spiroperidol binding to rat caudate nucleus homogenates after 3 to 10 weeks of haloperidol treatment was studied. Results confirmed previous reports that 3 weeks of haloperidol treatment leads to a significant increase in the number of receptor binding sites. The increase was more marked after 10 weeks of treatment and was accompanied by a significant increase in the variance of the number of receptor sites. Some Ss of the genetically heterogeneous rat strain developed a 400% increase over the number of dopamine receptors in the control group. This heterogeneity in individual response to neuroleptic treatment may be similar to the clinical situation in tardive dyskinesia which develops in only a fraction of treated patients. 16 references.

001200 Edelfors, Sven. Dept. of Pharmacology, University of Copenhagen, 20 Juliane Maries Vej, DK-2100 Copenhagen O, Denmark **The effect of lithium on the incorporation of 32P-orthophosphate into synaptosomal phospholipids from rat brain.** *Acta Pharmacologica et Toxicologica*. 46(2):133-137, 1980.

The effects of lithium treatment on the incorporation of 32P-orthophosphate into phospholipids of male Wistar rat synaptosomes were examined. In both lithium containing and lithium free media, 32P incorporation was lower in synaptosomes of rats given lithium in the diet for 5 weeks than in control rats. Results indicate that lithium treatment in vivo decreases the 32P incorporation into synaptosomal phospholipids and that this effect persists after removal of the lithium ion. 26 references. (Author abstract modified)

001201 Edstrom, J. P.; Phillis, J. W. Phillis: Dept. of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N 0W0 **A cholinergic projection from the globus pallidus to cerebral cortex.** *Brain Research*. 189(2):524-529, 1980.

A hypothesized cholinergic projection from the globus pallidus (GP) to the cortex of the rat was tested via stimulation of the GP while recording in the cortex, and a determination was made of the effect of iontophoresed acetylcholine (ACh) antagonists on the responses obtained. Recordings were obtained from 145 cells in 34 rats. Two types of response to stimulation of the GP and adjacent areas were observed: the first resembles the effect of stimulating the internal capsule, cerebral cortex, or thalamus and is probably due to current spread to the internal capsule; at lower stimulus strengths, a second specific response was encountered only in cells deeper than 1 mm. Both muscarinic and nicotinic antagonists were able to block parts of this short latency response. The most susceptible part of the response to cholinergic blockers was the inhibitory phase, with established cholinergic blockers failing to completely or reliably block the excitatory effect of GP stimulation. 28 references.

001202 Edvinsson, Lars; Larsson, Bengt; Skarby, Tor. Dept. of Histology, University of Lund, Biskopsgatan 5, S-223 62 Lund, Sweden **Effect of the GABA receptor agonist muscimol on regional cerebral blood flow in the rat.** *Brain Research.* 185(2):445-448, 1980.

To assess a possible involvement of GABA receptors in cerebral circulation, rat in vivo preparation was utilized to measure regional cerebral blood flow with the (14C)ethanol technique before and after treatment with the potent GABA receptor agonist, muscimol. Muscimol, administered i.v., caused a significant increase in blood flow of cortical brain regions. Blood flow measured in caudate nucleus, thalamus, mesencephalon, and cerebellum was not significantly altered by muscimol. Results give further support of a significant role of GABA mechanisms operating in cerebral circulation 16 references.

001203 Ehle, Albert L. Dept. of Neurology, University of Texas Health Science Center, Dallas, TX 75235 **Effects of phenytoin on amygdaloid kindled seizures in the rat.** *Electroencephalography and Clinical Neurophysiology.* 48(1):102-105, 1980.

The effects of oral phenytoin (0.25g/kg) on the evolution of amygdaloid seizures were examined in kindled male Sprague-Dawley rats. At blood levels within the human therapeutic range, phenytoin produced a 23% increase in threshold for afterdischarge and generalized seizures in fully kindled rats. Afterdischarge was blocked in half the animals after phenytoin was started when the stimulation intensity increased, but the treated animals developed generalized seizures in the same manner as controls. 13 references.

001204 Ehler, Frederick J.; Roeske, William R.; Rosenberger, Lois B.; Yamamura, Henry I. Dept. of Pharmacology, University of Arizona Health Sciences Center, Tucson, AZ 85724 **The influence of guanyl-5'-yl imidodiphosphate and sodium on muscarinic receptor binding in the rat brain and longitudinal muscle of the rat ileum.** *Life Sciences.* 26(3):245-252, 1980.

The effects of guanyl-5'-yl imidodiphosphate (Gpp(NH)p) and sodium on muscarinic receptor binding in the rat brain and longitudinal muscle of rat ileum were investigated using 3H(-)-quinclidiny benzilate ((3H)-QNB). When measured by competitive inhibition of (3H)-QNB binding to homogenates of the longitudinal muscle of the ileum, the IC50's of oxotremorine and carbachol increased by a factor of three in the presence of 30mM Gpp(NH)p. In contrast, Gpp(NH)p only produced small increases in IC50 values when binding experiments were done on various rat brain regions. Agonist inhibition curves deviated from the law of mass action and were consistent with a two binding site model. Variation was found in the percentage of high affinity agonist sites in the cerebellum (68%), brainstem (68%), longitudinal muscles of ileum (44% to 50%), and forebrain (21% to 30%). The predominant effect of Gpp(NH)p on agonist binding in ileum and forebrain was a reduction in the affinity of the high affinity binding site; no effect was found in cerebellum and brainstem. A preferential reduction of agonist affinity by sodium was observed in homogenates of forebrain and longitudinal muscle of the ileum. 21 references. (Author abstract modified)

001205 Eisenberg, Richard M. Dept. of Pharmacology, University of Minnesota, Duluth, School of Medicine, Duluth, MN 55812 **Effects of naloxone on plasma corticosterone in the opiate-naive rat.** *Life Sciences.* 26(12):935-943, 1980.

The effects of high doses of naloxone HCl (NX) (2.0 to 20.0mg/kg) on changes in plasma corticosterone were examined in the opiate naive rat. Using male rats with chronic intravenous catheters and one way vision boxes, injections were made and

serial blood samples were obtained in the conscious, unrestrained animal. The acute administration of NX to the opiate naive animal produced a dose related increase in plasma corticosterone with respect to both amplitude and duration. NX produced a significant elevation in hormone level at 15 and 30 minutes. With higher doses of NX, the duration of the response was extended to 60 minutes. To examine whether short-term tolerance to this effect could be produced, animals were given a single pretreatment with either NX or saline. Two hours later, NX produced a similar elevation in hormone level in both groups. The effect of chronic injection on NX was also studied. Animals pretreated with either NX or saline once daily for 7 days did not show a significant difference following the subsequent administration NX. In both cases, a significant elevation of plasma corticosterone resulted. The results suggest that NX may have a direct effect on opiate receptors resulting in an elevation of plasma hormone levels or NX may be disrupting an endogenous opiate receptor interaction producing a stress response. 38 references. (Author abstract modified)

001206 Elferink, J. G. R. Laboratory of Medical Chemistry, University of Leiden, Wassenaarseweg 72, 2333 AL Leiden, The Netherlands **Chlorpromazine inhibits phagocytosis and exocytosis in rabbit polymorphonuclear leukocytes.** *Biochemical Pharmacology.* 28(7):965-968, 1979.

Phagocytosis of zymosan particles and the concomitant release of lysosomal enzymes by exocytosis in rabbit polymorphonuclear leukocytes was inhibited by chlorpromazine. Cytochalasin-B prevented particle uptake, but not enzyme release. The divalent cation ionophore A23187 induced enzyme release in the absence of zymosan if calcium was present. In both cases, enzyme release was inhibited by chlorpromazine, indicating the effect of chlorpromazine on exocytosis is independent of its effect on phagocytosis. Results are discussed in relation to the role of calcium ions in exocytosis and the effect of chlorpromazine on membrane properties. 31 references. (Author abstract)

001207 Elias, Elwyn; Boyer, James L. Liver Study Unit, Yale University School of Medicine, New Haven, CT 06510 **Chlorpromazine and its metabolites alter polymerization and gelation of actin.** *Science.* 206(4425):1404-1406, 1979.

The effects of chlorpromazine and its metabolites on polymerization and gelation of actin were investigated. It was found that hepatic hydroxylated metabolites of chlorpromazine produce solid gel formation with filamentous actin, but the less toxic chlorpromazine sulfoxide metabolite did not. At higher concentrations, chlorpromazine inhibits actin polymerization. These dose response relationships parallel the drug's hepatic toxicity in vivo and suggest that interactions between chlorpromazine or chlorpromazine metabolites and actin could be an underlying mechanism of cell injury. 34 references. (Author abstract modified)

001208 Emery, Donna; Engel, Jorgen; Larsson, Knut. Dept. of Pharmacology, Box 33031, S-40033, Göteborg, Sweden **Rat strain differences in brain monoamine metabolism following para-chlorophenylalanine treatment.** *Pharmacology Biochemistry and Behavior.* 12(2):311-312, 1980.

The effect of parachlorophenylalanine (PCPA) on 5-hydroxytryptamine (5-HT) was studied in sham operated and castrated rats of two different rat strains. PCPA was more effective in depressing the brain 5-HT levels in Wistar rats than in Sprague Dawley rats. Assuming that the masculine sexual behavior of the rat is under inhibitory influence of 5-HT neuronal mechanisms, it is reasonable to expect that rats which are particularly sensitive to PCPA biochemically also show an increased behavior

ioral responsiveness to this treatment. 6 references. (Author abstract modified)

001209 Eskrom-Jodal, Barbro; Elfverson, Jorgen; von Essen, Claes. Elfverson: Department of Neurosurgery, Sahlgrenska sjukhuset, S-413 45 Göteborg, Sweden **Cerebral blood flow, cerebrovascular resistance, cerebral metabolic rate of oxygen and intracranial pressure during and after severe prolonged arterial hypoxia in dogs. The role of dopamine in the deep hypoxic state.** *Acta Neurologica Scandinavica*. 60(1):36-49, 1979.

The effect of extreme, prolonged arterial hypoxia on cerebral blood flow, oxygen uptake, and intracranial pressure was studied in anesthetized dogs. The experiments were performed along two lines. Both started with a period of hypoxia of about 40 minutes to 2 hours, and thereafter normoxia was reconstituted in one group and the animals were studied for another 1 to 2 hours. In the other group with continued hypoxia, dopamine was administered. During the hypoxic period the cerebral blood flow decreased mainly as a result of vasoconstriction after an initial marked flow increase. Cerebral oxygen uptake was reduced; intracranial pressure increased, largely in proportion to blood flow changes, and no indication of important brain edema appeared. In the recovery period at normoxia, the cerebral oxygen uptake showed an increase during the observation time. The blood flow, initially high, returned to the control level within the observation period. Dopamine infusion during continued hypoxia induced a vasodilatation, with reduction of vascular resistance to the values found at the induction of hypoxia, and with an increase of the cerebral oxygen uptake. An important role of endogenous dopamine in the hypoxic vasodilatation is suggested. 34 references. (Author abstract)

001210 Evans, M. H. A.R.C. Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England **Vasoactive sites in the diencephalon of the rabbit.** *Brain Research*. 183(2):329-340, 1980.

Vasoactive sites in the diencephalon of the rabbit were examined. Stimulation of the brainstem of the anesthetized rabbit, in the lateral hypothalamic area and the zona incerta 0.5 to 3mm from the midline and a similar distance dorsal to the lateral mammillary nucleus, evoked vasoconstriction in the skin of the ear and of the hindpaw. Only weak and inconstant effects on muscle blood flow were evoked from this region of the brainstem. Muscle vasodilatation was obtained by stimulation of more medial regions of the brainstem, extending almost all the way from the supramammillary nucleus to the dorsal surface. This vasodilatation was not diminished by atropine. Alpha-adrenergic blocking agents diminished the cutaneous vasoconstrictor responses and also reduced or even reversed the bradycardia that could be evoked by hypothalamic stimulation. 46 references. (Author abstract modified)

001211 Fahn, Stanley; Comi, Richard; Snider, Stuart R.; Prasad, A. L. N. Dept. of Neurology, Columbia University, College of Physicians and Surgeons, New York, NY 10032 **Effect of a catechol-O-methyl transferase inhibitor, U-0521, with levodopa administration.** *Biochemical Pharmacology*. 28(7):1221-1225, 1979.

Male Sprague-Dawley rats treated with the catechol-O-methyltransferase inhibitor, 3,4-dihydroxy-2-methyl-propriophenone (U-0521) and L-DOPA showed elevated levels of plasma and brain DOPA and brain dopamine, reduced plasma and brain levels of 3-O-methyl-DOPA (OMD), and reduced levels of brain homovanillic acid (VHA), compared to rats treated with L-DOPA alone. Plasma and brain OMD accumulation were inhibited when U-0521 (100mg/kg i.p.) was given 30 minutes prior to L-DOPA; brain VHA accumulation was also inhibited with

doses of 200mg/kg or higher. Results indicate that U-0521 blocks formation of O-methylated metabolites of L-DOPA and dopamine peripherally and centrally after high doses of L-DOPA and may be useful in treating Parkinsonism. 34 references. (Author abstract modified)

001212 Faingold, C.L. Division of Pharmacology, Dept. of Medical Sciences, Southern Illinois University, School of Medicine, Springfield, IL 62702 **Enhancement of mesencephalic reticular neuronal responses to sensory stimuli with pentylenetetrazol.** *Neuropharmacology*. 19(1):53-62, 1980.

The effects of pentylenetetrazol (PTZ) on the responses of mesencephalic reticular formation (MRF) neurons of the cat to visual, auditory, and somatosensory stimuli were studied. Subconvulsant doses of PTZ caused more than 90% of MRF neurons that had been unresponsive to sensory stimuli to become abruptly responsive to stimuli in at least one modality. PTZ also enhanced the responses of more than 90% of previously responsive MRF neurons. Following termination of PTZ administration, the responses of these neurons gradually returned to pre-drug patterns. These changes in MRF were correlated with PTZ-induced changes in MRF sensory evoked potential changes. Response attenuation (habituation) observed in MRF neurons appeared to be reversed by PTZ administration in some cases. These effects on MRF neurons may be involved in the seizure mechanisms of PTZ and other convulsant drugs. 32 references. (Author abstract modified)

001213 Fairchild, M. D.; Jenden, D. J.; Mickey, M. R.; Yale, C. Veterans Administration Hospital, Long Beach, CA 90822 **EEG effects of hallucinogens and cannabinoids using sleep-waking behavior as baseline.** *Pharmacology Biochemistry and Behavior*. 12(1):99-105, 1980.

Long-term EEG effects of hallucinogens (LSD, mescaline, psilocybin) and cannabinoid derivatives (tetrahydrocannabinol: THC, and synhexyl) were investigated in cats, using sleep/waking behavior as baseline. The drug induced alterations in the EEG frequency spectrum were drug specific in the sense that they would be statistically unlikely to occur during sleep/waking behavior. The two classes of compounds produced distinctly different EEG effects which were remarkably similar within each class. The duration of activity and relative potencies were consistent with those obtained by other measures, both in cats and in other species including man. 32 references. (Author abstract modified)

001214 Fairhurst, Alan S.; Whittaker, Michael L.; Ehler, Frederick J. Dept. of Medical Pharmacology and Therapeutics, University of California, Irvine, CA 92717 **Interactions of D600 (methoxyverapamil) and local anesthetics with rat brain alpha-adrenergic and muscarinic receptors.** *Biochemical Pharmacology*. 29(2):155-162, 1980.

D600 (methoxyverapamil) was found to inhibit the specific binding assayed in rat brain homogenates of the antagonist agents (3H)WB4101 and (3H)QNB to the alpha-adrenergic and muscarinic receptors, respectively. Scatchard analyses showed these inhibitions to be competitive. Lidocaine and tetracaine also competitively inhibited radioligand binding to these receptors. Increasing the Ca concentration in the assays to 10 mM did not influence the effects of D600 or the anesthetics. Analyses of inhibitions of muscarinic receptor binding produced by D600 and lidocaine over a range of pH indicated that the inhibitory species of D600 and lidocaine with the agonist site on the muscarinic receptor were studied by measuring the effects of these agents on the displacement of (3H)QNB by the muscarinic agonist carbachol. Comparison of these results with a theoretical model indicates that carbachol, (3H)QNB, and D600 or lido-

caine competitively displace one another at the same agonist site. The binding of labeled naloxone to the opiate receptor was also inhibited by D600. These inhibitory effects of D600 and the local anesthetics on different receptors suggest that these agents may act by a common mechanism, namely by perturbing membrane structures. These results suggest caution in interpreting experiments in which D600 and verapamil are used analytically as Ca antagonists to assess the involvement of Ca in a biological system. 23 references. (Author abstract modified)

001215 Feenstra, Matthijs G. P.; Rollema, Hans; Horn, Alan S.; Dijkstra, Durk; Grof, Cor J.; Westerink, Ben H. C.; Westerbrink, Aaf. Lab of Pharmaceutical and Analytical Chemistry, State University of Groningen, Ant. Deusinglaan 2, 9713 AW Groningen, The Netherlands **Effect of dihydroxy-2-aminotetralin derivatives on dopamine metabolism in the rat striatum**. *Naunyn-Schmiedeberg's Archives of Pharmacology*. 310(3):219-225, 1980.

Concentrations of dopamine (DA), dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) were measured in the striatum of rats after i.p. injection of apomorphine, N,N-dipropylamine and a series of alkylated and/or esterified dopamine analogues of the dihydroxyaminotetralin type. All compounds tested caused a decrease in DOPAC and HVA concentrations.

N,N-dipropylamino-5,6-dihydroxytetrahydronaphthalene (DiPr-5,6-ADTN) was found to be the most potent compound, with a maximal effect at a dose of 0.33mmol/kg, it being 30 times more potent than apomorphine and DiPr-6,7-ADTN. The results corroborate reported behavioral data, and the relative potencies of the alkylated derivatives in this test system for dopaminergic activity are in agreement with those based on stereotyped behavior. 42 references. (Author abstract modified)

001216 Feldman, Jerome M.; Blalock, Judith A. Durham Veterans Administration Medical Center, Durham, NC 27710 **The role of altered tissue norepinephrine concentration in the hereditary obese-hyperglycemic syndrome of mice**. *Research Communications in Chemical Pathology and Pharmacology*. 26(3):479-493, 1979.

Treatment of normal and obese C56BL/6J mice with the monoamine oxidase inhibitorspargiline or clorgyline for 25 weeks resulted in significant inhibition of monoamine oxidase in the hypothalamus, cerebral cortex, kidney, heart, and epididymal fat. The norepinephrine concentration was significantly increased in the hypothalamus of the normal mice and in the cerebral cortex of the obese mice. The obese mice given clorgyline showed an increase in plasma glucose (313mg/dl) over the obese mice given saline (167mg/dl). However, the increase in tissue norepinephrine did not result in increased weight gain or alterations in organ weights. Results suggest that the elevated hypothalamic norepinephrine concentration normally seen in the hereditary obese/hyperglycemic mouse is probably not the cause of their obesity. 29 references. (Author abstract modified)

001217 Felner, Aina E.; Waldmeier, Peter C. Waldmeier: Research Dept., Pharmaceuticals Division, Ciba-Geigy Ltd., Basel, Switzerland **Cumulative effects of irreversible MAO inhibitors in vivo**. *Biochemical Pharmacology*. 28(7):995-1002, 1979.

The effects of repeated treatment with clorgyline, pargyline, deprenyl, and tranlylcypromine on monoamine oxidase (MAO) activity in rat brain and liver were investigated, using 5-hydroxytryptamine (5-HT), phenethylamine (PEA), and tyramine as substrates. Single subcutaneous doses of clorgyline (1 and 10mg/kg) completely blocked the deamination of 5-HT; PEA deamination decreased gradually during 14 day treatment. Pargyline (0.3mg/kg) reduced both 5-HT and PEA deamination

progressively over the same period. In the course of repeated treatment, the effects of clorgyline and deprenyl on 5-HT and PEA deamination increased in intensity by a factor of about 10 in the brain and about 3 in the liver; the potentiation of the effect of tranlylcypromine was less marked. Rates of recovery of MAO activity were not greater after repeated injections of high doses of clorgyline and deprenyl than after single injections, suggesting that the withdrawal of these drugs is not followed by a rebound phenomenon. Results indicate that repeated treatment with suitable doses of clorgyline or deprenyl leads to specific reduction of MAO-A or MAO-B activity in brain, without producing appreciable effects in the liver. 16 references. (Author abstract modified)

001218 Fertel, R. H.; Greenwald, J. E.; Schwarz, R.; Wong, L.; Bianchine, J. Dept. of Pharmacology, Ohio State University, Columbus, OH 43210 **Opiate receptor binding and analgesic effects of the tetrahydroisoquinolines salsinol and tetrahydropapaveroline**. *Research Communications in Chemical Pathology and Pharmacology*. 27(1):3-16, 1980.

The opiate binding and analgesic effects of salsinol (SAL) and tetrahydropapaveroline (THP) were studied in male Sprague-Dawley rats. Both tetrahydroisoquinolines bound to brain opiate receptors. Sodium ions (100mM) caused a four fold decrease in the ability of SAL and THP to displace tritiated naloxone binding. THP and SAL both had antinociceptive effects in the tail flick test after intraventricular administration. Their potency was comparable to that of the enkephalins, and their effects were blocked by naloxone. 23 references. (Author abstract modified)

001219 Feuerstein, Giora; Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Effect of PGD2, PGE2, PGF2alpha and PGI2 on blood pressure, heart rate and plasma catecholamine responses to spinal cord stimulation in the rat**. (Unpublished paper). Bethesda, MD, NIMH, 1980. 15 p.

The interrelationships of various prostaglandins (PGs) and the adrenergic nervous system, in conjunction to blood pressure and heart rate responses, were studied in vivo in rats. Stimulation of the entire spinal cord of the pithed rat increased blood pressure, heart rate, and plasma epinephrine (EPI) and norepinephrine (NE) concentration (radioenzymatic/thin layer chromatographic assay). Infusion of PGE2 suppressed blood pressure and heart rate responses to spinal cord stimulation while plasma EPI (but not NE) was augmented over levels found in control animals. PGI2 suppressed the blood pressure response to spinal cord stimulation without any effect on heart rate or the plasma catecholamine levels. PGD2 and PGF2alpha did not change the blood pressure, heart rate, or plasma EPI and NE responses to the spinal cord stimulation although PGF2alpha disclosed an overall vasopressor effect at the prestimulation period. At the prestimulation period it was also observed that PGE2, PGF2alpha, and PGI2 had a direct positive chronotropic effect on the heart rate. These in vivo studies suggest that in the rat PGE2 and PGI2 modulate sympathetic responses, primarily by interaction with the postsynaptic elements, PGE2 on both blood vessels and the heart rate and PGI2 by acting principally on blood vessels. 23 references. (Author abstract modified)

001220 Fields, H. L.; Emson, P. C.; Leigh, B. K.; Gilbert, R. F. T.; Iversen, L. L. MRC Neurochemical Pharmacology Unit, Dept. of Pharmacology, University of Cambridge, Medical School, Hills Road, Cambridge CB2 2QD, England **Multiple opiate receptor sites on primary afferent fibres**. *Nature*. 284(5754):351-353, 1980.

The distribution and binding characteristics of opiate receptors on rat dorsal root and in various regions of the adjacent

spinal cord were examined using the selective radioligands 3H-morphine (micro sites) and 3H-D-Ala2,D-Leu5-enkephalin (delta sites). Primary afferent tissue (dorsal root) and dorsal horn were found to contain micro delta opiate binding sites with relatively high proportion of micro sites. Partial destruction of small diameter primary afferents after cutting the sciatic nerve led to a significant reduction in both micro binding sites and delta binding sites on dorsal roots, suggesting that both types of opiate receptors may exist on small diameter primary afferents. 29 references. (Author abstract modified)

001221 Figge, James; Leonard, Paul; Richelson, Elliott. Richelson: Dept. of Pharmacology, Mayo Foundation, Rochester, MN 55901 **Tricyclic antidepressants: potent blockade of histamine H1 receptors of guinea pig ileum.** *European Journal of Pharmacology*. 58(4):479-483, 1979.

Six tricyclic antidepressants were tested for their ability to antagonize histamine actions at histamine H1-receptors in a bioassay for these receptors (histamine-induced contractions of guinea-pig ileum). Doxepin, amitriptyline, imipramine, nortriptyline, protriptyline, and desipramine all acted as competitive antagonists; doxepin and amitriptyline were the most potent compounds in the series. Antagonism at histamine H1-receptors may account for the sedative effects of these tricyclic compounds. 11 references. (Author abstract modified)

001222 File, Sandra E.; Hyde, J. R. G. Dept. of Pharmacology, School of Pharmacy, University of London, 29-39 Brunswick Square, London WC1N 1AX, England **Evidence that Piracetam has an anxiolytic action.** *Journal of Affective Disorders* 1(4):227-235, 1979.

Evidence is presented that Piracetam (100mg/kg) has an anxiolytic profile similar to that seen after 5 days of chlordiazepoxide (5mg/kg) administration in the social interaction test of anxiety. Piracetam (50 to 300mg/kg) produced no signs of sedation in previous tests, and the suggestion that it might be a non-sedative anxiolytic drug was investigated. A 100mg/kg dosage in male rats produced significantly higher cortical concentrations of 5-hydroxytryptamine and lower concentrations of 5-hydroxyindoleacetic acid indicating a reduced 5-HT turnover. There were no drug-induced changes in noradrenaline or dopamine in any brain region, either with or without pretreatment with alpha-methylparatyrosine. The cortical concentrations of seven amino acids were measured and were unchanged by Piracetam treatment. 34 references. (Author abstract modified)

001223 Filion, Michel. Laboratoires de Neurobiologie, Hôpital de l'Enfant-Jésus, Pavillon Notre-Dame, Québec G1J 5B3, Canada **Effects of interruption of the nigrostriatal pathway and of dopaminergic agents on the spontaneous activity of globus pallidus neurons in the awake monkey.** *Brain Research*. 178(2-3):425-441, 1979.

The spontaneous activity of globus pallidus neurons was recorded in intact *Macaca mulatta* and in monkeys with lesions of the ventromedial midbrain tegmentum. In intact monkeys, medial pallidus neurons discharged uninterruptedly at high firing rates; the discharge of most lateral pallidus neurons was interrupted by relatively long periods of silence. Lesions of the nigrostriatal pathway altered the firing patterns but not the mean firing rates of pallidus neurons. In lesioned monkeys, pallidus neurons fired in bursts continuously during movement, rest, and sleepiness. The percentage of bursting pallidus neurons was proportional to the amount of degeneration in the pars compacta of the ipsilateral substantia nigra. The bursting activities seen in lesioned animals could be reproduced in intact monkeys by chronic administration of the dopamine antagonists haloperidol and reserpine. Single injections of the dopamine agonists apomorphine

and pibedil silenced the medial pallidum and abolished the signs of parkinsonism in the lesioned monkeys. 52 references. (Author abstract modified)

001224 Finnegan, Kevin Toth. University of Chicago **Tolerance and dopamine depletions after the repeated administration of d-methylamphetamine.** (Ph.D. dissertation). Dissertation Abstracts International. 40(8):4016-B, 1980. (Not available from Univ. Microfilms), 1979.

The relationship between the depletion of caudate dopamine and d-methylamphetamine (d-MA) tolerance was examined by comparing the effects of d-MA, apomorphine, and haloperidol on monkeys' lever-pressing behavior maintained by food delivered on a differential reinforcement of low rate schedule (DRL) before and after a period of repeated d-MA administration. After completion of the behavioral investigations all monkeys were sacrificed and their brains neurochemically analyzed. Monkeys repeatedly injected with d-MA developed a tolerance to the behaviorally disruptive effects of this drug, as well as a long-lasting depletion of caudate dopamine. It is suggested that the mechanism concerned in the development of d-MA tolerance involves a reduction of functional dopaminergic transmission. (Journal abstract modified)

001225 Finnerty, Edward P.; Chan, Samuel H. H. Chan: Dept. of Life Sciences, Indiana State University, Terre Haute, IN 47809 **Morphine suppression of substantia nigra zona reticulata neurons in the rat: implicated role for a novel striatonigral feedback mechanism.** *European Journal of Pharmacology*. 59(3/4):307-310, 1979.

In lightly anesthetized male rats, systemic administration of morphine produced a naloxone reversible suppression of the spontaneous or dopamine enhanced firing of neurons in the substantia nigra zona reticulata. It is suggested that inactivation of these neurons within the striatonigral pathway may complement a direct action of the opiate on the nigrostriatal dopaminergic cells, resulting in the morphine suppression of caudate neuronal activities. Morphine may disinhibit the dopamine containing cells of the zona compacta by depressing inhibitory neurons in this novel striatonigral mechanism. 9 references. (Author abstract modified)

001226 Fitz, J. Gregory; McNamara, James O. Duke University Medical Center, Durham, NC 27710 **Muscarinic cholinergic regulation of epileptic spiking in kindling.** *Brain Research*. 178(1):117-127, 1979.

Electroencephalographic monitoring of spontaneous interictal spiking (SIS) following kindling in male Sprague-Dawley rats demonstrated that SIS occurs in both amygdala and declines sharply during the days following kindling. Systemic administration of the muscarinic agonists atropine and scopolamine activated interictal spiking in kindled rats but not in controls. Interictal spiking activated by atropine was reversed by physostigmine. Physostigmine and choline, which increase brain acetylcholine (ACh) concentrations by different mechanisms, both caused a reduction in spontaneous interictal spiking. Results suggest that the interaction of endogenous ACh with central muscarinic receptors is capable of suppressing SIS in kindled rats. 19 references. (Author abstract modified)

001227 Fleissner, A.; Bremkamp, H.; Seifert, R. Psychiatrische und Nervenkrankheiten der Universität Hamburg, Martinistrasse 52, D-2000 Hamburg 20, Germany **In vitro haemolysis from adrenochrome in the blood of schizophrenic patients, revised.** *Archiv für Psychiatrie und Nervenkrankheiten*. 226(4):341-346, 1979.

The recently reported abnormal in vitro haemolysis from catecholamine metabolites in schizophrenia (Hegedus and Alts-

chule, 1970) was tested with 62 subjects. The influence of plasma substitution by Ringer solution in incubation samples was studied. The postulated increase in haemolysis was not found, though the exchange of plasma for Ringer solution renders some patients' erythrocytes more susceptible to the effects of adrenochrome. It is concluded that if findings concerning the dopamine hypothesis of schizophrenia were, in a subgroup, the results of a slightly altered aminochrome metabolism, erythrocytes would be a suitable object in which to study the underlying disorders in this subgroup of schizophrenics. 6 references.

001228 Fludder, Joan M.; Leonard, B. E. MRC Toxicology Unit, Carshalton, SM5 4EF, England **The effects of amitriptyline, mianserin, phenoxybenzamine and propranolol on the release of noradrenaline in the rat brain in vivo.** *Biochemical Pharmacology*. 28(15):2333-2336, 1979.

The postsynaptic adrenoceptor antagonists phenoxybenzamine increased the concentration of normetanephrine in the male Wistar rat amygdaloid cortex following acute administration, but chronic phenoxybenzamine treatment had no effect and chronic propranolol treatment decreased concentrations of this metabolite in the amygdaloid cortex. Acute administration of the presynaptic alpha-adrenoceptor agonist clonidine decreased the concentration of normetanephrine in the amygdaloid cortex, whereas the blockade of presynaptic adrenoceptors with yohimbine increased normetanephrine concentration. The antidepressants amitriptyline and mianserin also increased normetanephrine concentrations. When given in combination with clonidine, yohimbine and mianserin both antagonized the clonidine-induced decrease in normetanephrine concentrations. Amitriptyline did not antagonize the effect of clonidine, suggesting it does not affect noradrenaline release by acting on presynaptic neurotransmitter release mechanisms. 27 references. (Author abstract modified)

001229 Fowler, Christopher J.; Ekstedt, Bertil; Egashira, Toru; Kinemuchi, Hiroyasu; Orelund, Lars. Dept. of Pharmacology, University of Umea, S-901 87 Umea, Sweden **The interaction between human platelet monoamine oxidase, its monoamine substrates and oxygen.** *Biochemical Pharmacology*. 28(20):3063-3068, 1979.

The interaction of human platelet monoamine oxidase (MAO) type-B with beta-phenethylamine, tryptamine, and benzylamine substrates was examined. Treatment with pargyline, thermal denaturation, and 2-butanone affected enzyme activity to the same degree with all three amine substrates. Mixed substrate experiments indicated the substrates inhibit each other in a competitive manner. The activity of MAO-B increased in an uncompetitive manner when the oxygen concentration was raised, but the degree of increase was dependent on the substrate used in the assay. Results suggest that MAO human platelet MAO-B has a single binding site for amine substrates but may have more than one binding site for oxygen. 35 references. (Author abstract modified)

001230 Francis, Andrew; Jagannath, Anand; Schechter, Nissim. Schechter: Dept. of Psychiatry, Health Sciences Center, SUNY, Stony Brook, NY 11794 **Stability of muscarinic-cholinergic receptor activity in the deafferented retinotectal pathway.** *Brain Research*. 185(1):161-168, 1980.

The high affinity muscarinic antagonist 3-quinuclidinyl benzilate was used to analyze muscarinic cholinergic receptor activity in the optic tectum of goldfish and optic lobe of developing chicks and adult pigeons after deafferentation. In contrast to the loss of nicotinic cholinergic receptor binding activity seen in previous experiments with alpha-bungarotoxin, no significant loss of total or specific muscarinic receptor binding activity was

observed. The stability of the muscarinic site relative to the nicotinic site is discussed. 30 references. (Author abstract modified)

001231 Francis, Andrew; Schechter, Nissim. Schechter: Long Island Research Institute, Health Sciences Center T-10, SUNY, Stony Brook, NY 11794 **Putative cholinergic receptor activity in the deafferented rat superior colliculus.** *Brain Research*. 183(1):224-228, 1980.

Nicotinic and muscarinic cholinergic receptor activity was studied in the deafferented superior colliculus of male Sprague-Dawley rats. Eye removal produced a 15% decrease in alpha-bungarotoxin binding activity, but did not alter quinuclidinyl benzilate binding. These findings are consistent with those obtained in other species. The stability of the muscarinic receptors suggests they are not present on the presynaptic element of retinotectal terminals, but are located on systems not subject to degradation during optic denervation of the colliculus. 23 references.

001232 Fredholm, Bertil B.; Hjelm Dahl, Paul; Hammarstrom, Sven. Dept. of Pharmacology, Karolinska Institutet, Stockholm, Sweden **Stimulation and inhibition of cyclic AMP formation in isolated rat fat cell by prostacyclin (PGI₂).** *Biochemical Pharmacology*. 29(4):661-663, 1980.

The stimulation and inhibition of cyclic AMP (cAMP) formation in isolated rat fat cell by prostacyclin (PGI₂) were investigated. Results demonstrate that low doses of PGI₂ potentiate cAMP accumulation induced by several concentrations of noradrenaline (NA). Conversely, higher doses inhibited cAMP accumulation induced by NA, except when the effect of NA was antagonized by NG-phenylisopropyl adenosine (PIA), in which case PGI₂ had no further inhibitory effect. Data indicate that PGI₂ in a low concentration range may enhance rather than inhibit NA-induced cAMP accumulation, although the effect is small. Even though PGI₂ is more potent than PGE₂ on vascular relaxation, blood platelets and human lymphocytes, this order of potency is not universal. This suggests that there are differences in ligand affinity of prostaglandin receptors in different tissues. There appears to be little reason to change the previous negative conclusions concerning the physiological importance of prostaglandins as negative feedback regulators in adipose tissue. 15 references.

001233 Freed, William J.; Nasrallah, Henry A.; Rogol, Alan D.; Wyatt, Richard J. Lab. of Clinical Psychopharmacology, Division of Special Mental Health Research, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Propranolol in high doses increases plasma prolactin concentrations in male rats.** *Biological Psychiatry*. 15(2):311-317, 1980.

The effects of propranolol in high doses on the plasma prolactin concentrations in male Sprague-Dawley albino rats were examined. Amounts over 50mg/kg were found to greatly increase plasma prolactin. Propranolol alters several physiological systems in both the peripheral and central nervous systems that may explain this effect. It is concluded that for both the neuroleptics and propranolol there is an intriguing correspondence between therapeutic effects and concentrations of propranolol in rat blood. 21 references.

001234 French, Edward D. Arthur V. Davis Center for Behavioral Neurobiology, Salk Institute, La Jolla, CA 92037 **Dexamethasone blocks morphine-induced hyperthermia in restrained rats.** *Life Sciences*. 25(18):1583-1589, 1979.

Morphine (30mg/kg i.p.) produced a marked hyperthermia in male Sprague-Dawley rats in small plexiglass restraining cages, but caused a pronounced hyperthermia in unrestrained rats. The absolute magnitude and time course for these effects were simi-

lar in the two groups. In restrained rats pretreated with dexamethasone, the hypothermic responses to morphine was prevented and a subsequent hyperthermia was observed. In unrestrained rats, dexamethasone slightly attenuated the morphine-induced hyperthermia. Results indicate that restraint is a potent modifier of morphine's effects on thermoregulation, probably as a result of stress related activation of anterior pituitary hormone release. The possibility that stress-induced release of adrenocorticotrophic hormone or beta-endorphin is involved in this modification is discussed. 24 references. (Author abstract modified)

001235 Freye, E.; Arndt, J. O. Institute für Anesthesiologie der Universität Düsseldorf, Gebäude 23.02.01, Universitätsstrass 1, D-4000 Düsseldorf, Germany **Perfusion of the fourth cerebral ventricle with fentanyl induces naloxone-reversible bradycardia, hypotension, and EEG synchronisation in conscious dogs.** Naunyn-Schmiedeberg's Archives of Pharmacology. 307(2):123-128, 1979.

Perfusion of increasing concentrations (2.5 to 20mcg/ml) of fentanyl through the fourth cerebral ventricle of conscious dogs resulted in a concentration related fall in heart rate, an inhibition of the reflex response of heart rate to carotid clamping, and a moderate fall in blood pressure. Fourth ventricle perfusion of fentanyl also induced a gradual synchronization of the EEG, with delta activity corresponding to behavioral signs of tranquilization and sleep-like states. All these effects were reversed by naloxone. No effects were seen when fentanyl was perfused through the lateral ventricles and third ventricle, even though this procedure yielded serum drug concentrations similar to those obtained after perfusion of the fourth ventricle. It is concluded that opiate receptors bordering the fourth cerebral ventricle mediate the cardiovascular and hypnotic actions of fentanyl. 33 references. (Author abstract modified)

001236 Fried, P. A.; Charlebois, A. T. Carleton University, Ottawa, Ontario, Canada **Effects upon rat offspring following Cannabis inhalation before and/or after mating.** Canadian Journal of Psychology. 33(3):125-132, 1979.

The timing of fetal exposure to cannabinoids was studied with rats exposed to marihuana smoke during the entire gestation period, prior to mating, or both prior to and during gestation. Cannabis inhalation in gravid rats on days 1 to 19 of gestation resulted in offspring that were smaller at birth, had delayed physiological development, and were less active than control pups. Administering the Cannabis for 19 days before mating and continuing during gestation attenuated the drug effects, which was interpreted as suggesting a mechanism of tolerance in the dam. Cannabis exposure limited to 19 days prior to mating in either males or females did not produce marked postnatal effects in offspring but, in both cases, the resulting litters contained twice as many males as females. 35 references. (Author abstract modified)

001237 Fried, P. A.; Charlebois, A. T. Carleton University, Ottawa, Ontario, Canada **Cannabis administered during pregnancy: first- and second-generation effects in rats.** Physiological Psychology. 7(3):307-310, 1979.

The reproductive organs and fertility of animals born to rats that were exposed to cannabis smoke throughout gestation were examined and the second generation rats were tested for evidence of frank and subtle teratogenesis. Female rats were administered cannabis smoke or placebo smoke throughout gestation, and the offspring were injected with tetrahydrocannabinol (THC) 2 months prior to mating. The male and female offspring of the experimental animals were significantly less fertile and had smaller reproductive organs. The experimental F2 generation weighed less and were slower in some aspects of physio-

logical development compared to F2 control animals. Exposure to cannabis smoke as a fetus and THC as a young adult had a much greater effect on fertility than just injections of THC 2 months prior to mating. 35 references. (Author abstract modified)

001238 Friedman, Allan H.; Davis, James N. Neurology Research Laboratory, Veterans Administration Medical Center, Durham, NC 27705 **Identification and characterization of adrenergic receptors and catecholamine-stimulated adenylate cyclase in hog pial membranes.** Brain Research. 183(1):89-102, 1980.

Catecholamine stimulated adenylate cyclase activity and the binding of tritiated dihydroalprenolol (3H-DHA) and dihydroergocryptine (3H-DHE) were studied in membranes prepared from the hog pia. The binding of 3H-DHA was saturable (0.09pmol/mg protein) with a high affinity (10nM). The receptor binding appeared to be composed largely of beta2-adrenergic sites, but some sites with beta1-adrenergic properties were detected. The beta-adrenergic agonist isoproterenol stimulated adenylate cyclase activity by 20% in pial membranes in the presence of guanosine triphosphate. The potency of catecholamines in stimulating adenylate cyclase activity correlated well with their ability to compete for 3H-DHA binding. The binding of 3H-DHE was also saturable (0.39pmol/mg protein) on these membranes. Alpha-adrenergic agents were potent competitors for 3H-DHE binding, but dopamine, serotonin, and histamine were effective only at high concentrations. Results demonstrate presence of alpha-adrenergic and beta-adrenergic membrane receptors and beta-adrenergically stimulated adenylate cyclase activity in small pial blood vessels in the hog. 48 references. (Author abstract modified)

001239 Friedman, David Paul. New York Medical College **Norepinephrine and dopamine: their role in electrocortical activation. A neuropharmacological study.** (Ph.D. dissertation). Dissertation Abstracts International. 39(11):5254-B, 1979. Ann Arbor, Univ. Microfilms No. 7910263, 245p., 1978.

Elicited synchrony and activation were used to study the manner in which changes in the synaptic availability of norepinephrine (NE) and dopamine (DA) affect arousal. The caudate nuclei of cats were stimulated to elicit spindles and the mesencephalic reticular formations (MRF) were stimulated to induce activation. Changes in the threshold for eliciting spindles and in their amplitude and duration were used as indirect measures of tonic levels of activation. Thresholds required to block spindles and the duration of the blockade obtained with suprathreshold stimuli were used to assess more phasic aspects of elicited activation. Results suggest that interactions of DA and NE containing neuronal systems may be the important variable to consider when effects on arousal are evaluated. DA appears to be the more important catecholamine in the mediation of arousal; its action is supported and complemented by NE. (Journal abstract modified)

001240 Fromm, Gerhard H.; Glass, Jay D.; Chattha, Amrik S.; Martinez, A. Julio; Silverman, Michael. Dept. of Neurology, University of Pittsburgh, School of Medicine, Pittsburgh, PA 15261 **Antibabes drugs and inhibitory pathways.** Neurology. 30(2):126-131, 1980.

The actions of known anticonvulsant drugs on normal cat synaptic systems were investigated. Conditioning stimuli to the coronal gyrus or periventricular gray matter inhibit the activity of spinal trigeminal neurons. Valproate decreased the corticofugal inhibition of the spinal trigeminal nucleus, as did ethosuximide, trimethadione, and imipramine. Valproate and ethosuximide also decreased the periventricular inhibition of the spinal trigeminal nucleus, indicating that antibabes drugs depress

subcortical inhibitory pathways as well as pathways of cortical origin. These results support the hypothesis that ability to depress inhibitory pathways is an important characteristic of anti-tic drugs. The effect of valproate and ethosuximide on periventricular inhibition also suggests that these anticonvulsants may act by preventing the spread of seizure activity through subcortical pathways. 48 references. (Author abstract modified)

001241 Fukumori, Ryuji; Minegishi, Akemi; Satoh, Tetsuo; Kitagawa, Haruo; Yanaura, Saizo. Satoh: Dept. of Biochemical Pharmacology, Faculty of Pharmaceutical Sciences, Chiba University, Yayoi-cho 1-33, Chiba 260, Japan **Effects of barbital and disulfiram on the metabolism of intracerebroventricularly administered (14C)-5-hydroxytryptamine in rats**. Research Communications in Chemical Pathology and Pharmacology. 26(1):217-220, 1979.

One hour after intracerebroventricular injection of 14C-labelled 5-hydroxytryptamine (5-HT), the levels of total and deaminated radioactive materials were higher in male Wistar rats treated with barbital or disulfiram than in controls. An additive effect was observed with combined administration of the two drugs. Results suggest that barbital and disulfiram inhibit the metabolism of 5-hydroxyindoleacetaldehyde, a first deaminated metabolite in 5-HT metabolism. 11 references. (Author abstract modified)

001242 Fukumori, Ryuji; Minegishi, Akemi; Satoh, Tetsuo; Kitagawa, Haruo; Yanaura, Saizo. Satoh: Dept. of Biochemical Pharmacology, Faculty of Pharmaceutical Sciences, Chiba University, Yayoi-cho 1-33, Chiba, Japan **Synergistic effect of prostaglandin E1 and disulfiram on the prolongation of hexobarbital hypnosis**. Brain Research. 181(1):241-244, 1980.

Hexobarbital hypnosis in male Wistar rats was prolonged by pretreatment with prostaglandin-E1 (PGE1, 1mg/kg i.p.) or disulfiram (200mg/kg i.p.). Combined administration of the two drugs prolonged hexobarbital hypnosis and drastically reduced brain hexobarbital content on awakening. PGE1 enhanced 5-hydroxytryptamine synthesis without altering the elimination of 5-hydroxyindoleacetic acid. Results suggest that elevation of the steady state level of 5-hydroxyindoleacetaldehyde potentiates hexobarbital hypnosis. 13 references.

001243 Fuller, R. W.; Snoddy, H. D.; Perry, K. W. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Nisoxetine antagonism of norepinephrine depletion in brain and heart after alpha-methyl-m-tyrosine administration**. Neuropharmacology. 18(10):767-770, 1979.

Nisoxetine hydrochloride (5 to 40mg/kg i.p.) antagonized the depletion of norepinephrine (NE) in brain and heart following the subcutaneous injection of alpha-methyl-m-tyrosine (AMMT, 6.25 to 100mg/kg) in male Wistar rats and Cox mice. In rats, the degree of antagonism was directly related to the dose of nisoxetine and inversely related to the dose of AMMT. Nisoxetine also reduced the tissue concentration of metaraminol, the AMMT metabolite whose retention in nerve terminals probably accounts for the depletion of NE. Nisoxetine significantly antagonized the depletion of brain NE and decreased the retention of metaraminol when metaraminol itself was injected. Results indicate that nisoxetine effectively antagonizes uptake into noradrenergic neurons in vivo, which may account for the drug's clinical antidepressant activity. 11 references. (Author abstract modified)

001244 Fuller, Ray W.; Hemrick, Susan K.; Molloy, Bryan B.; Day, William A. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46385 **Inhibition of rat brain norepinephrine N-methyltransferase in vitro and in vivo by chloro-substi-**

tuted 1-aminoindans. Research Communications in Chemical Pathology and Pharmacology. 27(3):485-495, 1980.

Norepinephrine N-methyltransferase (NMT) from male Wistar rat brains was inhibited in vitro by 1-aminoindans with chlorine substituent on the aromatic ring. The most potent compound, 4,5-dichloro-1-aminoindan, was a competitive inhibitor in kinetic studies with L-norepinephrine as the variable substrate. At doses of 10 to 40mg/kg i.p., this compound also inhibited brainstem and hypothalamic NMT activity in vivo and lowered hypothalamic concentrations of epinephrine for several hours. Results suggest that 4,5-dichloro-1-aminoindan may be a useful tool in studies of epinephrine forming neurons in brain. 9 references. (Author abstract modified)

001245 Fuller, Ray W.; Mason, Norman R.; Molloy, Bryan B. Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN 46206 **Structural relationships in the inhibition of (3H)serotonin binding to rat brain membranes in vitro by 1-phenyl-piperazines**. Biochemical Pharmacology. 29(5):833-835, 1980.

The inhibition of (3H)serotonin binding by a series of substituted 1-phenyl-piperazines is described. Various 1-phenyl-piperazines and related compounds were shown to be effective in inhibiting the binding of (3H)serotonin to rat brain membranes in vitro. The most effective compound was 1-(m-trifluoromethylphenyl)-piperazine. Variation in the piperazine moiety of this compound greatly diminished the ability of this compound to inhibit (3H)serotonin binding. Some variation in the nature of the meta substituent retained activity but compounds with substituents in other positions of the phenyl ring were less active. 20 references.

001246 Fuller, Ray W.; Molloy, Bryan B.; Hemrick, Susan K.; Perry, Kenneth W. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Inhibition of rat brain norepinephrine N-methyltransferase by 2,3,4,5-tetrahydro-1H-indeno (1,2-c)pyridine hydrochloride (LY87130)**. Brain Research. 190(1):215-223, 1980.

Inhibition of rat brainstem norepinephrine N-methyltransferase (NMT) by 2,3,4,5-tetrahydro-1H-indeno (1,2-c)pyridine Hydrochloride (LY87130) was studied in vitro. Epinephrine concentration in hypothalamus was lowered within 1 hour after LY87130 injection; the lowering was maximum at 6 hours and persisted at 24 but not 48 hours after a 40mg/kg dose of LY87130. MOPEG sulfate, a major metabolite of norepinephrine in rat brain, was markedly elevated by LY87130. The effects of low doses of LY87130 were enhanced by ipindole, which increased LY87130 levels in the brain, suggesting that ring hydroxylation is a major pathway of LY87130 metabolism. The ability of LY87130 to produce selective depletion of epinephrine in rat brain makes it a useful tool for manipulating epinephrine forming neurons. 33 references. (Author abstract modified)

001247 Fuxe, Kjell; Hall, Hakan; Kohler, Christer. Dept. of Histology, Karolinska Institutet, Stockholm, Sweden **Evidence for an exclusive localization of 3H-ADTN binding sites to postsynaptic nerve cells in the striatum of the rat**. European Journal of Pharmacology. 58(4):515-517, 1979.

The distribution of binding sites for tritiated (●)-6,7-dihydroxy-2-aminotetralin (3H-ADTN) was examined in male Sprague-Dawley rats with unilateral cortical ablations or various brain lesions induced by the neurotoxins ibotenic acid and 6-hydroxydopamine (6-OHDA). The cortical ablations did not significantly alter 3H-ADTN binding. Ibotenic acid-induced lesions of the striatum almost totally eradicated specific 3H-ADTN binding sites, even though 3H-spiperone binding was reduced by only 45% under the same conditions; maximum 3H-ADTN

binding capacity was reduced on the lesioned side with no change in affinity. Following 6-OHDA-induced lesions of ascending dopaminergic pathways, there was a small, nonsignificant (27%) increase in 3H-ADTN binding sites with no change in affinity. Results suggest that the 3H-ADTN sites are located almost exclusively on postsynaptic nerve cell elements in the striatum and have no direct relationship to the 3H-spiperone binding sites located on axon terminals in the striatum. 5 references.

001248 Gale, Karen. Dept. of Pharmacology, Georgetown University Schools of Medicine and Dentistry, 3900 Reservoir Road, Washington, DC **Chronic blockade of dopamine receptors by antischizophrenic drugs enhances GABA binding in substantia nigra.** *Nature*. 283(5747):569-570, 1980.

The effects of chlorpromazine and haloperidol on specific GABA binding in the substantia nigra and striatum of rats were investigated and compared with those of clozapine, an antischizophrenic drug with an atypical biochemical and clinical profile. Data support the hypothesis that chronic blockade of dopamine receptors by classical antischizophrenic drugs enhances GABA binding in the substantia nigra. This effect may be related to the extrapyramidal side-effects associated with classical antischizophrenic drug treatment. 40 references. (Author abstract modified)

001249 Gallagher, Dorothy W.; Bunney, William E., Jr. Clinical Center, Rm. 2N315, Section on Biochemistry and Pharmacology, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Failure of chronic lithium treatment to block tricyclic antidepressant-induced 5-HT supersensitivity.** *Naunyn-Schmiedeberg's Archives of Pharmacology*. 307(2):129-133, 1979.

The effect of chronic lithium administration on the supersensitivity to 5-hydroxytryptamine (5-HT) induced by tricyclic antidepressants was investigated in male Sprague-Dawley rats. Administration of chlorimipramine of imipramine for 14 days resulted in a five fold increase in the sensitivity of hippocampal pyramidal cells to iontophoretically applied 5-HT. This supersensitivity was not blocked by concurrent administration of lithium. Results indicate that the blockade of supersensitivity to dopamine induced by lithium can not be generalized to all central amine systems. 31 references. (Author abstract modified)

001250 Gallagher, Dorothy W.; Mallorga, Pierre. Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20205 **Diphenylhydantoin: pre- and postnatal administration alters diazepam binding in developing rat cerebral cortex.** *Science*. 208(4439):64-66, 1980.

The effects of diphenylhydantoin (DPH) on benzodiazepine binding at various stages of neuronal maturation in the rats were examined and these effects were compared to the development of the anticonvulsant activity of DPH. Also, the effect of exposure in utero to DPH on benzodiazepine binding in maturing rats was studied. Close correlations between the development of the anticonvulsant effects of DPH and increases in tritiated diazepam binding were observed in rats from fetal day 16 to maturation. In contrast, significant decreases in tritiated diazepam binding were observed in 2-week-old and 3-week-old rats that were exposed in utero to DPH. These changes can be correlated with reported increases in seizure susceptibility after prenatal exposure to DPH. 13 references. (Author abstract modified)

001251 Gallagher, Joel P.; Inokuchi, Hiroe; Shinnick-Gallagher, Patricia. Dept. of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77550 **Dopamine depolarisation of mammalian primary afferent neurones.** *Nature*. 283(5749):770-772, 1980.

In a series of experiments, the effects of dopamine (D/A) on cat dorsal root ganglion were examined. Preliminary results of studies of DA-induced depolarization using voltage clamp techniques indicate that, unlike GABA-induced depolarization, chloride was not involved, whereas a decreased potassium conductance is at least contributory. DA at various concentrations produced similar slow membrane depolarizations in 75% of the cells to which it was applied, but in no instance did it hyperpolarize the membrane. Apomorphine was at least twice as effective as DA in causing membrane depolarization; and both apomorphine and DA produced sustained nondesensitizing depolarizations for as long as the drug was in contact with the preparation. Of the drugs tested, only chlorpromazine and haloperidol antagonized the action of DA. Although noradrenaline (N/A) depolarized the membrane, it did not depolarize it to the same degree as DA even at ten times the concentration of DA. NA-induced depolarization could not be antagonized by phentolamine. Propanolol was also ineffective in blocking the action of the amines. Adrenaline and serotonin were less effective depolarizing agents than NA; and isoprenaline did not depolarize. 23 references.

001252 Galvan, M.; Grafe, P.; ten Bruggencate, G. Dept. of Physiology, University of Munich, Pettenkoferstrasse 12, D-8000 Munich 2, Germany **Facilitatory actions of guanidine on synaptic transmission in mammalian brain slices.** *Experimental Neurology*. 67(1):234-246, 1980.

The effects of guanidine on neuronal properties and synaptic transmission in isolated slices of guinea-pig olfactory cortex were studied using intracellular and extracellular recording methods. Addition of guanidine to the superfusate produced the following effects: excitatory and inhibitory postsynaptic potentials, evoked by stimulation of the lateral olfactory tract, were increased in amplitude and duration; the amplitude and frequency of spontaneously occurring postsynaptic potentials were significantly increased; membrane potential and input resistance remained virtually unchanged; and the duration of the lateral olfactory tract compound action potential was prolonged. These results suggest that guanidine enhances the release of excitatory and inhibitory neurotransmitters in the mammalian cortex and this effect may be beneficial in human central nervous system diseases in which the efficiency of synaptic transmission is reduced. 32 references. (Author abstract modified)

001253 Garcia-Sevilla, J. A.; Magnusson, T.; Carlsson, A. Magnusson, Dept. of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg, Sweden **Effects of enkephalins and two enzyme resistant analogues on monoamine synthesis and metabolism in rat brain.** *Naunyn-Schmiedeberg's Archives of Pharmacology*. 310(3):211-218, 1980.

The effects of enkephalins on brain monoamine turnover were assessed. Methionine-enkephalin and leucine-enkephalin increased the accumulation of 3,4-dihydroxyphenylalanine (DOPA) by a naloxone sensitive mechanism in different rat brain regions after inhibition of the aromatic L-amino acid decarboxylase. The two enzyme resistant enkephalin analogues D-Ala²-methionine enkephalin amide (DALA and FK 33-824) also increased the synthesis of DOPA, dose dependently and by naloxone sensitive mechanism, but at a much lower dosage level. The effects of enkephalins and enkephalin analogues on brain tyrosine concentration, and on formation of 5-hydroxytryptophan are also reported. All four peptides accelerated the disappearance of dopamine, noradrenaline and 5-hydroxytryptamine after inhibition of monoamine synthesis. The results suggest that endogenous enkephalins, through the activation of opiate receptors, are involved in the short-term regulation of central monoaminergic systems. 32 references. (Author abstract modified)

001254 Garrett, Edward R.; Jackson, Andre J. Beehive, College of Pharmacy, J. Hillis Miller Health Center, University of Florida, Gainesville, FL 32610 **Pharmacokinetics of morphine and its surrogates III: morphine and morphine 3-monoglucuronide pharmacokinetics in the dog as a function of dose.** *Journal of Pharmaceutical Sciences*. 68(6):753-771, 1979.

The pharmacokinetics of morphine and its derived metabolite, morphine 3-monoglucuronide, were studied in normal and bile cannulated dogs. High i.v. doses (7.2 to 7.7mg/kg) caused renal and biliary shutdowns and time lags in urinary drug and metabolite excretion and in biliary secretion of the hepatically formed conjugate. Intermediate doses (0.41 to 0.47mg/kg) inhibited urine flow but not renal clearance. Low doses (0.019 to 0.07mg/kg) had no apparent effect. Bile cannulated dogs showed no fecal elimination of drug and no slow terminal plasma and urine elimination phases. Morphine 3-monoglucuronide was eliminated only renally. 30 references. (Author abstract modified)

001255 German, Dwight C.; Dalsass, Mario; Kiser, R. Sanford. Dept. of Physiology, University of Texas Health Science Center, Dallas, TX 75235 **Electrophysiological examination of the ventral tegmental (A10) area in the rat.** *Brain Research*. 181(1):191-197, 1980.

Responses of neurons in the ventral tegmental (A10) area of female rats were examined following electrical stimulation of the nucleus accumbens (NA) and olfactory tubercle (OT). Results showed that the A10 dopaminergic (DA) neurons could be antidromically activated from synaptic terminal regions in the NA and OT. The firing rate of these cells was reduced by dopaminergic drugs (apomorphine, amphetamine, and amfonelic acid), and this was reversed by DA antagonists (haloperidol and chlorpromazine). Many A10 cells were inhibited by NA stimulation, and this response occurred at a lower threshold than that required for antidromic activation. 24 references.

001256 Gershon, Michael D.; Dreyfus, Cheryl F. Dept. of Anatomy, Columbia University College of Physicians and Surgeons, New York, NY 10032 **Stimulation of tryptophan uptake into enteric neurons by 5-hydroxytryptamine: a novel form of neuromodulation.** *Brain Research*. 184(1):229-233, 1980.

The effect of 5-hydroxytryptamine (5-HT) on the uptake of L-tryptophan was examined in strips of longitudinal muscle with adherent myenteric plexus (LM-MP strips) from 32 male guinea-pigs. 5-HT significantly enhanced the uptake of L-tryptophan and this action of 5-HT was found to probably involve the release of a neurotransmitter. This enhancement of the uptake of L-(3H)tryptophan by 5-HT is blocked by tetrodotoxin, Ca²⁺ free, or high (30 microM) Mg²⁺ solutions. It is concluded that the enhanced uptake of L-(3H)tryptophan appears to be a neuromodulatory effect of 5-HT involving the activation of at least one intermediate neuron which in turn releases a neurotransmitter that acts on the neurons (probably serotonergic) responsible for L-(3H)tryptophan uptake. 12 references.

001257 Geyer, Mark A. Dept. of Psychiatry (T-004), University of California, San Diego, La Jolla, CA 92093 **Both indoleamine and phenylethylamine hallucinogens increase serotonin in both dorsal and median raphe neurons.** *Life Sciences*. 26(6):431-434, 1980.

The effects of representative indoleamine and phenylethylamine hallucinogens on both dorsal and median raphe neurons were compared using a newly developed cytofluorimetric technique for the detection of changes in intracellular serotonin levels in the brains of male Sprague/Dawley rats. The results suggest that indoleamine and phenylethylamine hallucinogens are similar in their effects on both of the major midbrain raphe

nuclei. The selective increase in intracellular serotonin levels may reflect the inhibition of firing of serotonin neurons produced by these drugs. 14 references.

001258 Gintzler, Alan R. Dept. of Anatomy, Columbia University, College of Physicians and Surgeons, New York, NY 10032 **Substance P involvement in the expression of gut dependence on opiates.** *Brain Research*. 182(1):224-228, 1980.

The role of substance-P in mediating the naloxone-induced atropine resistant contraction of gut taken from chronically morphinized guinea-pigs was examined. In the absence of specific substance-P antagonists, desensitization to substance-P was used to demonstrate a pharmacological response mediated by this peptide. Desensitization did not appreciably affect contractile responses to acetylcholine, histamine, potassium chloride, or electrical stimulation. In contrast, desensitization to substance-P markedly reduced the magnitude of the atropine resistant contractile response to naloxone, suggesting substance-P participates in mediating the response. 19 references.

001259 Giorgiuffi-Chesselet, M. F.; Kemel, M. L.; Wandscheer, D.; Glowinski, J. Group NB, INSERM U.114, College de France, 11, place Marcelin Berthelot, F-75231 Paris cedex 5, France **Glycine stimulates the spontaneous release of newly synthesized 3H-dopamine in rat striatal slices.** *European Journal of Pharmacology*. 60(1):101-104, 1979.

Glycine stimulated the spontaneous release of tritiated dopamine (DA) continuously synthesized from tritiated tyrosine in Sprague-Dawley rat striatal slices. This effect was calcium dependent and significantly reduced in the presence of strychnine. The glycine evoked release of 3H-DA was abolished in the presence of tetrodotoxin. These findings provide preliminary evidence for the existence of glycinergic neurons that interact with dopaminergic terminals in the striatum. 10 references. (Author abstract modified)

001260 Glass, Jay D.; Fromm, Gerhard H.; Chattha, Amrik S. Dept. of Pharmacology, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261 **Bicuculline and neuronal activity in motor cortex.** *Electroencephalography and Clinical Neurophysiology*. 48(1):16-24, 1980.

Application of microgram quantities of bicuculline to the precruciate gyrus (motor cortex) of cats increased visually evoked and spontaneous unit activity. A surface negative component of the slow wave response was markedly enhanced by bicuculline. This component was associated with an intense suppression of spontaneous single unit activity. It is concluded that bicuculline has a convulsant effect on single unit neuron activity and also potentiates a process that appears to be associated with an enhancement of inhibition. 36 references.

001261 Glennon, Richard A. Dept. of Pharmaceutical Chemistry, School of Pharmacy, Virginia Commonwealth University, Richmond, VA 23298 **A similarity between rat fundus serotonin receptors and brain serotonin binding sites.** *Research Communications in Psychology, Psychiatry and Behavior*. 4(3):333-336, 1979.

The rat fundus serotonin (5-HT) receptor affinities of several compounds are compared with the concentrations of these agents necessary to inhibit specific 5-HT binding to calf brain homogenates by 50%. Results of comparison by linear regression analysis of bufotenine, 5-methoxy-N,N-dimethyltryptamine, psilocin, N,N-dimethyltryptamine, tryptamine and quipazine (whose binding affinities span approximately 2 orders of magnitude) show a correlation in the ability of this series of compounds to interact with rat fundus 5-HT receptors and calf brain 5-HT binding sites. The gross structure/activity relationships in-

dependent of preparation of the compared compounds are discussed. 13 references. (Author abstract modified)

001262 Glick, S. D.; Cox, R. D.; Meibach, R. C. Dept. of Pharmacology, Mount Sinai School of Medicine, City University of New York, 1 Gustave L. Levy Place, New York, NY 10029 Selective effect of reinforcing doses of morphine in striatum. *Brain Research*. 190(1):298-300, 1980.

The labeled deoxyglucose technique was employed to assess changes in functional activity in different brain regions of rats self-administering morphine. The results implicate the striatum in the mechanism of morphine reinforcement. The selective increase in deoxyglucose activity reported here is to be contrasted with the widespread depression in activity reported to occur after much larger doses of morphine. It is suggested that the deoxyglucose technique can, perhaps, be most profitably used to explore sites of drug action when reference is made to a particular effect and dosages are chosen accordingly. 10 references.

001263 Gnagy, M. E.; Lau, Y. S. Dept. of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48109 Effects of chronic and acute treatment of antipsychotic drugs on calmodulin release from rat striatal membranes. *Neuropharmacology*. 19(3):319-323, 1980.

Possible alteration in calmodulin release from the striatal membranes caused by chronic and acute treatment with antipsychotic drugs was investigated in rats. Chronic treatment with haloperidol and (-)-butaclamol results in supersensitivity of striatal dopamine (DA) receptors. Striatal membranes of these Ss have an increased calmodulin content. Both endogenous and protein kinase induced release of calmodulin from striatal membranes is substantially lower than that of saline or (-)-butaclamol treated Ss. Acute treatment produces no alteration in calmodulin content or calmodulin release from the membranes. The impaired calmodulin release seen in the chronic antipsychotic treated Ss could be associated with the supersensitivity of DA receptors. 10 references. (Author abstract modified)

001264 Gogan, F.; Rotsztein, W. H.; Couturier, L.; Chazal, G.; Beattie, I.; Kordon, C. Unite de Neuroendocrinologie (U. 159), Centre Paul Broca de l'INSERM, 2ter rue d'Alesia, F-75014 Paris, France Interaction of the anti-estrogen CI-628 and estradiol on plasma LH and hypothalamic LH-RH in the female rat. *Brain Research*. 184(1):109-118, 1980.

The effects of the interaction of the antiestrogen CI-628 and estradiol (E2) on the plasma LH and hypothalamic LH-RH in the female rat were examined. Increasing doses of CI-628 induced a dose dependent inhibition of (3H)E2 retention in both cytosolic and nuclear fractions of the pituitary. In contrast, hypothalamic retention of (3H)E2 is only inhibited significantly with higher doses of CI-628 (2.4 and 24mg/kg). In the presence of E2, CI-628 has both estrogenic and antiestrogenic properties on LH secretion. It is concluded that CI-628 acts at the pituitary level to decrease the tissue sensitivity to LH-RH, but has no effect on mediobasal hypothalamic LH-RH content. 42 references. (Author abstract modified)

001265 Gothoni, Patrick; Ahtee, Liisa. Division of Pharmacology, Dept. of Pharmacy, University of Helsinki, Kirkkokatu 20, SF-00170, Helsinki 17, Finland Chronic ethanol administration decreases 5-HT and increases 5-HIAA concentration in rat brain. *Acta Pharmacologica et Toxicologica*. 46(2):113-120, 1980.

The effect of acute and chronic ethanol administration on cerebral 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) concentrations of male Sprague-Dawley and Wistar rats was studied. Acute ethanol administration caused a slight (13%) fall in 5-HT concentration and a slight (10%) in-

crease in 5-HIAA concentration 1 hour after administration. In chronically treated rats, whole brain 5-HT decreased by 9% during ethanol intoxication; this fall was significant in the part of the brain containing the diencephalon, mesencephalon, and telencephalon except cortex (23% decrease) and in that containing pons and medulla oblongata (37% decrease), but not in cerebral cortex. Cerebral 5-HIAA concentrations of chronically treated animals were increased during intoxication and withdrawal by 24 to 58% in all three sections. Since ethanol did not enhance the probenecid-induced elevation of cerebral 5-HIAA, ethanol apparently increases cerebral 5-HIAAS by attenuating its removal from brain. 13 references. (Author abstract modified)

001266 Grace, Anthony A.; Bunney, Benjamin S. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 Paradoxical GABA excitation of nigral dopaminergic cells: indirect mediation through reticulata inhibitory neurons. *European Journal of Pharmacology*. 59(3/4):211-218, 1979.

Single unit recording techniques revealed a population of neurons in the zona reticulata (ZR) of the male Sprague-Dawley rat substantia nigra that was 20 times more sensitive than neurons of the zona compacta (ZC) to iontophoretically applied GABA. Microiontophoretic application of GABA in the ZR caused an increase in ZC cell activity, but glutamic acid produced a picrotoxin reversible inhibition of the ZC cells. Muscimol (i.v.) caused a decrease in ZR cell activity at the same dose that caused a parallel increase in ZC cell firing rate. Results suggest that ZC cells receive inhibitory GABA input from ZR cells, which are in turn inhibited by low doses of GABA agonists. This anatomical arrangement could account for the paradoxical excitatory effect of GABA agonists on dopaminergic cells in the ZC. 34 references. (Author abstract modified)

001267 Grahame-Smith, D. G. MRC Unit of Clinical Pharmacology, Radcliffe Infirmary, Oxford OX2 6HE, England The effects of drugs on the processes regulating the functional activity of brain monoamines. *Progress in Neuro-Psychopharmacology*. 3(1-3):15-23, 1979.

The effects of certain drugs on the synthesis and turnover of brain monoamines and the study of these effects with the use of behavioral models which indicate the functional activity of brain serotonin and dopamine, are reviewed. Using these techniques, the acute and chronic effects of certain neuroleptics, propranolol and other beta-adrenergic blocking agents, repeated electroconvulsive shock, and lithium upon the functional activity of brain serotonin and dopamine are examined. The clinical relevance of these studies is discussed. 22 references. (Author abstract modified)

001268 Grandison, Lindsey; Guidotti, Alessandro. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 Role of the anterior pituitary GABA receptor in the control of prolactin release. (Unpublished paper). Washington, DC, NIMH, 1979. 11 p.

Evidence is presented for an involvement of the GABAergic system in hypothalamic pituitary function (actions of the GABA mimetic muscimol on prolactin (PRL) release and pituitary GABA receptors). The data demonstrate that muscimol, a GABA mimetic, potentially inhibits PRL release. The ineffectiveness or slight stimulatory action of centrally injected muscimol and its poor penetration into the CNS suggested a pituitary site of action. This conclusion is supported by the ability of muscimol to inhibit PRL release when coincubated with anterior pituitary halves and by the presence of GABA binding sites in pituitary membrane fractions. Muscimol-induced inhibition of PRL

release occurs through GABA receptors since specific GABA receptor antagonists reverse its action. In addition, this GABA receptor mediated effect is independent of the dopaminergic inhibition of PRL. The pituitary cell type on which GABA mimetics act and the physiological significance of this inhibitory mechanism is being investigated. The preliminary data suggest that, if the results obtained in rodents can be confirmed in humans, then it can be anticipated that the effectiveness of muscimol or the more appropriate GABA mimetic compounds may be clinically useful to reduce PRL secretion during hyperprolactinemia and during treatment with neuroleptics. 36 references.

001269 Greenfield, Susan; Cheramy, Andre; Leviel, Vincent; Glowinski, Jacques. Groupe NB, INSERM U.114, Collège de France, 11, place Marcelin Berthelot, F-75231 Paris Cedex 05, France. *In vivo* release of acetylcholinesterase in cat substantia nigra and caudate nucleus. *Nature*. 284(5754):355-357, 1980.

To investigate the possible release of acetylcholine (AChE) from dopaminergic dendrites and terminals, the *in vivo* release of this enzyme from the substantia nigra and caudate nuclei of cats implanted with four push/pull cannulae was measured and compared with that of dopamine (DA). Spontaneous AChE release was observed in the substantia nigra and in the caudate nucleus. Moreover, the application of potassium chloride (30mM) in one substantia nigra increased the local release of AChE. This was accompanied by remote changes in the enzyme release from the other three structures which differed from that seen for DA. The different patterns of responses observed for AChE and DA suggest that AChE may also originate from other neurons in both the substantia nigra and the caudate nucleus. 25 references. (Author abstract modified)

001270 Greer, Charles A.; Alpern, Herbert P. Alpern: Dept. of Psychology, Muenzinger Building, University of Colorado, Boulder, CO 80309. *Paradoxical effects of d-amphetamine upon seizure susceptibility in 2 selectively bred lines of mice*. *Developmental Psychobiology*. 13(1):7-15, 1980.

The ontogeny and substrates of amphetamine-induced changes in flurothyl-induced myoclonic and clonic seizure thresholds were investigated in two selectively bred mouse lines. The long-sleep mice exhibited dose dependent increases in myoclonic and clonic susceptibility following amphetamine administration, regardless of age. However, the short-sleep mice exhibited a dichotomous myoclonic response to amphetamine that was age dependent. At earlier ages, amphetamine decreased seizure susceptibility, and at later ages it increased susceptibility. The results suggest that the short-sleep mice may be a naturally occurring animal model of preadolescent hyperkinesis. 23 references. (Author abstract modified)

001271 Griersmith, B. T.; Duggan, A. W. Dept. of Pharmacology, John Curtin School of Medical Research, Australian National University, Canberra, Australia. *Prolonged depression of spinal transmission of nociceptive information by 5-HT administered in the substantia gelatinosa: antagonism by methysergide*. *Brain Research*. 187(1):231-236, 1980.

Methysergide and lysergic acid diethylamide (LSD) were examined for possible antagonism of the prolonged depression of spinal transmission of nociceptive information by serotonin (5-HT) administered in the substantia gelatinosa (SG). Possible antagonism of the effects of 5-HT, administered electrophoretically in the cat SG, was studied on 27 neurons, 16 in lamina IV, 9 in lamina V, and 2 in lamina VI. When methysergide was administered after nociceptive responses to noxious heat stimuli had been depressed by 5-HT, no antagonism of the effects of 5-HT was observed. By contrast, when methysergide was adminis-

tered for 10 to 34 minutes prior to and concurrently with the administration of 5-HT, antagonism of the action of 5-HT was observed on 12 of 16 cells. It is noted that the prevention but not reversal of the action of 5-HT by methysergide is probably related to the hypothesized prolongation of the action of 5-HT beyond the period when 5-HT is present at its receptor. 32 references.

001272 Griffith, William H., III; Gallagher, Joel P.; Shinnick-Gallagher, Patricia. Dept. of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77550. *An intracellular investigation of cat vesical pelvic ganglia*. *Journal of Neurophysiology*. 43(2):343-354, 1980.

The use of intracellular recording techniques to study individual neurons in the cat parasympathetic vesical pelvic ganglion (VPG) is described, and the utility of the VPG model in the study of parasympathetic ganglionic transmission at the cellular level is assessed. Active and passive electrical properties were determined from 140 ganglion cells (35 preparations), and three types of ganglion cells were distinguished. Type I (A and B) cells were nonaccommodating cells in response to depolarizing current pulses. Type II cells showed accommodation to depolarizing current pulses. Type IB cells exhibited two kinds of non-synaptic spontaneous activity, spontaneous action potentials and small spontaneous potentials. The duration of the spikes after hyperpolarization resulting for either orthodromic or antidromic train stimulation was dependent on the frequency of train stimulation. Chlorisondamine, d-tubocurarine, and hexamethonium reversibly blocked orthodromic responses. 25 references. (Author abstract modified)

001273 Grinker, Joel A.; Drewnowski, Adam; Enns, Melvin; Kissileff, Harry. Rockefeller University, 1230 York Avenue, New York, NY 10021. *Effects of d-amphetamine and fenfluramine on feeding patterns and activity of obese and lean Zucker rats*. *Pharmacology Biochemistry and Behavior*. 12(2):265-275, 1980.

The effects of two doses of d-amphetamine and fenfluramine on male Zucker rats maintained ad lib on solid and liquid diets were investigated using the technique of meal pattern analysis. Amphetamine-induced anorexia was of short duration in both obese and lean rats. In the lean rats, anorexia was followed by rebound feeding resulting in little or no reduction in total daily intake. The drug reduced meal sizes of obese but not lean rats and caused a transient decrease in meal frequency. Increased spontaneous activity paralleled the decreased food intake. In contrast, anorexia following fenfluramine was greater, more prolonged, and of equivalent magnitude in obese and in lean rats. No rebound feeding was observed. Reduction in intake was achieved primarily by changes in meal size rather than in meal frequency. These data demonstrate the food intakes of genetically obese Zucker rats are more susceptible to the action of d-amphetamine than those of lean rats, and are consistent with reports of differential neurotransmitter levels in the obese and lean rats. 24 references. (Author abstract)

001274 Gruol, Donna L.; Barker, Jeffrey L.; Huang, Li-Yen Mae; MacDonald, J. Ferguson; Smith, Thomas G., Jr. A. V. Davis Center, Salk Institute, P.O. Box 85800, San Diego, CA 92138. *Hydrogen ions have multiple effects on the excitability of cultured mammalian neurons*. *Brain Research*. 183(1):247-252, 1980.

The effects of iontophoretically applied hydrogen ions (H) were studied in spinal neurons dissociated from 13-day-old mouse embryo and grown in culture for 1 to 6 months. H was able to activate transmitter-like conductances and to elevate the threshold for spike generation. Responses evoked by iontophoretic application of glutamate, glycine, and GABA were de-

pressed by H. Results indicate that H (a sudden increase in acidity) can evoke a topographically distributed, desensitizing, transmitter-like response in central neurons which may alter the findings of pharmacological studies in which drugs in acidic solutions are employed. 14 references.

001275 Gundersen, Cameron B.; Newton, Michael W.; Jenden, Donald J. Dept. of Pharmacology, UCLA School of Medicine, Los Angeles, CA 90024 **Beta-bungarotoxin elevates diaphragm acetylcholine levels.** *Brain Research.* 182(2):486-490, 1980.

The effects of beta-bungarotoxin (beta-BTX) on acetylcholine (ACh) metabolism in the rat diaphragm muscle were examined. Beta-BTX produced an increase in tissue ACh levels and a reduction in evoked ACh release. The time course of the rise in tissue ACh and the depression in ACh output were similar. These findings suggest that beta-BTX may cause a transient depolarization of nerve terminals that inhibits choline transport, rather than a sustained inhibitory effect on choline uptake. 18 references.

001276 Gurwitz, David; Kloog, Yoel; Egozi, Yaakov; Sokolovsky, Mordechai. Dept. of Biochemistry, George S. Wise Faculty of Life Sciences, Tel-Aviv University, Tel-Aviv, Israel **Central muscarinic receptor degeneration following 6-hydroxydopamine lesion in mice.** *Life Sciences.* 26(1):79-84, 1980.

Adult mice received two 70mcg doses of 6-hydroxydopamine intracisternally 72 hours apart, and the muscarinic binding properties of discrete brain regions were then investigated at various time intervals. Three days after the second injection, 3H-norepinephrine uptake was drastically reduced in all brain regions studied, and a distinct decrease in muscarinic receptor density was observed in the striatum, medulla pons, and cerebellum of lesioned animals as compared with controls. No changes were detected in muscarinic receptor density in the cortex or the hippocampus of treated animals, nor were any changes seen in the affinity of the labelled ligand for its receptor or in the displacement properties of the muscarinic binding by agonists in any of the regions studied. These effects still persisted after 60 days, with a further reduction in striatal muscarinic density to 74% of control values. Data are interpreted with respect to the proposed model for cholinergic modulation of central catecholamine release and cholinergic/catecholaminergic interactions in the striatum. 22 references. (Author abstract)

001277 Haga, Tatsuya; Haga, Kazuko. Department of Biochemistry, Hamamatsu University School of Medicine, Hamamatsu 431-31, Japan **Characterization of alpha-adrenergic receptor subtypes in rat brain: estimation of ability of adrenergic ligands to displace 3H-dihydroergocryptine from the receptor subtypes.** *Life Sciences.* 26(3):211-218, 1980.

A method for characterizing the alpha-adrenergic subtypes is reported which involves studying the displacement of 3H-dihydroergocryptine (DHE) by various adrenergic ligands in the absence and presence of prazosin and yohimbine. Two distinct alpha-adrenergic binding sites of DHE were observed in synaptic membranes of rat brain: one with a high affinity for prazosin (P-site); and others with a low affinity which appeared to consist of a site with high affinity for yohimbine (Y-site) and the other with a low affinity (X-site). The proportion of P, Y, and X-sites was estimated to be 25%, 27%, and 48% of specific binding sites of DHE. Norepinephrine, epinephrine, and clonidine were found to have higher affinities for Y and X-sites than for P-site; and indoramin had a much higher affinity for P-site. Methoxamine, phentolamine, and DHE had similar affinities for the three sites. Affinities of ligands for P-sites correlated closely with those of binding sites for 3H-WB-4101, and those for Y

and X-sites correlated with those for binding sites of 3H-clonidine. 16 references. (Author abstract modified)

001278 Hanbauer, I.; Costa, E. Section on Biochemical Pharmacology, Hypertension Endocrine Branch, National Heart, Lung, and Blood Institute, Bethesda, MD 20205 **Role of calmodulin in dopaminergic transmission.** (Unpublished paper). Bethesda, MD, NIMH, 1980. 37 p.

Experiments on rat brain tissue show that calmodulin appears to be involved in the regulation of dopamine receptor by acting at the cyclase and phosphodiesterase level. Dopamine receptor activation promotes translocation of calmodulin, dopamine receptor blockade facilitates accumulation of calmodulin on membranes. Cocaine and (d)-amphetamine differ on their actions on calmodulin: while (d)-amphetamine causes the changes expected from continuous stimulation of dopamine receptors, cocaine causes the changes expected from receptor blockade or denervation. It is suggested that this supersensitivity of dopamine receptors may play a role in determining the difference in the pharmacological profiles of (d)-amphetamine and cocaine. 56 references.

001279 Hanbauer, I.; Gimble, J.; Sankaran, K.; Sherard, R. Section on Biochemical Pharmacology, NHLBI, NIH, Bethesda, MD 20205 **Modulation of striatal cyclic nucleotide phosphodiesterase by calmodulin: regulation by opiate and dopamine receptor activation.** *Neuropharmacology.* 18(11):859-864, 1979.

Incubation of male Sprague-Dawley rat striatal slices with morphine increased the cytosolic content of calmodulin. The double reciprocal plot of cyclic AMP phosphodiesterase versus cyclic AMP concentration was biphasic with apparent high and low Michaelis-Menten constant (Km) forms in control slices, but was monophasic with only the low Km form in morphine exposed slices. The changes in apparent Km for cyclic AMP elicited by morphine were blocked by haloperidol and naltrexone. In slices prepared from deafferented caudate nuclei, morphine did not alter the biphasic double reciprocal plot, but incubation with dopamine caused the appearance of a low Km form of phosphodiesterase (PDE). Gel filtration of soluble extracts revealed significantly more calmodulin in the fraction containing PDE activity in the morphine treated slices than in control slices. Results suggest that opiate receptors may be located on dopaminergic neurons and that opiates may influence that regulation of PDE by calmodulin via postsynaptic receptors. Changes in PDE mediated by the increased availability of calmodulin can be used as an index of stimulation of dopamine receptors and may be related to the development of subsensitive receptor responses. 21 references. (Author abstract modified)

001280 Hanke, J.; Hofeler, H.; Krieglstein, J.; Wever, K. Krieglstein: Philipps-Universität, Ketzertbach 63, D-3550 Marburg/Lahn, Germany **Influence of various lipophilic drugs on brain mitochondrial hexokinase.** *Naunyn-Schmiedeberg's Archives of Pharmacology.* 307(2):171-176, 1979.

The effects of various lipophilic drugs on male Sprague-Dawley rat brain mitochondrial hexokinase were examined in vivo and in vitro. Chlorpromazine, perphenazine, imipramine, and desipramine enhanced the binding of hexokinase to rat brain mitochondria in vitro, but did not alter the intracellular hexokinase distribution in cortex in vivo. Thiopental and the enantiomers of 1-methyl-5-phenyl-5-propylbarbituric acid produced a solubilization of hexokinase activity from brain mitochondria in vitro. In vivo, thiopental and the (R)(-)-enantiomer-induced anesthesia and an increase of soluble hexokinase activity in cortex, but the (S)(+)-enantiomer caused convulsions with no increase in soluble hexokinase activity in cortical tissue. Amphetamine, morphine, phenytoin, and tetracaine enhanced the mitochondrial

binding of hexokinase activity in rat cortex in vivo. Ethanol and phenytoin increased soluble activity in cortex in vivo, and phenylbutazone solubilized hexokinase activity only in vitro. Results suggest that in therapeutic doses, only the anesthetics solubilize hexokinase activity from mitochondrial in vivo and in vitro. 12 references. (Author abstract modified)

001281 Harris, F. A. Dept. of Physiology and Biophysics, University of Washington School of Medicine, Seattle, WA 98195 **Wide-field neurons in somatosensory thalamus of domestic cats under barbiturate anesthesia.** *Experimental Neurology*. 68:27-49, 1980.

A sample of 392 somatosensory thalamic neurons from barbiturate anesthetized cats, all responsive to stimulation of the contralateral forepaw (CFP), was compared with a previously described sample from chloralose anesthetized Ss. Focus was on the functional properties of CFP responsive neurons isolated within nucleus ventralis posterolateralis (VPL), the spatial distributions of distinguishable neuronal subsets within VPL, and the distribution of CFP evoked single unit discharge along the mediolateral dimension of the nucleus and over time. The results show a number of wide field, bilaterally excited neurons in the VPL of barbiturate anesthetized cats, and earlier descriptions with chloralose anesthetized cats cannot be discounted as having resulted from an artifact of anesthesia unique to the latter agent. 47 references. (Author abstract modified)

001282 Haubrich, Dean R.; Risley, Edwin A.; Williams, Michael. Neuropsychopharmacology Section, Merck Institute for Therapeutic Research, West Point, PA 19486 **Effects of deanol, choline and its metabolites on binding of (3H)quinuclidinyl benzilate to rat brain membranes.** *Biochemical Pharmacology*. 28(24):3673-3674, 1979.

The ability of deanol, choline, and some choline metabolites to displace labelled quinuclidinyl benzilate (QNB) was compared with cholinergic drugs in muscarinic receptors in rat brain preparations. Choline displaced QNB from its muscarinic binding site with an IC₅₀ of approximately 1800mM. Choline was less potent than the other muscarinic receptor agonists by a factor ranging from 20 for carbachol to 4,000 for oxotremorine. The IC₅₀ value for scopolamine was more than 100,000 times as potent as choline. Choline was three times as potent as deanol, and two to five times as potent as any of its metabolites. The finding that choline and deanol displace QNB is consistent with previous studies showing that these compounds stimulate cholinergic receptors at high concentrations. However, the fact that choline and its metabolites were considerably less potent than cholinomimetic drugs in displacing QNB indicates that the central cholinergic actions of choline cannot be attributed entirely to direct activation of these receptors. 14 references.

001283 Hayes, Ann G.; Tyers, Michael B. Tyers: Pharmacology Dept., Glaxo Group Research Ltd., Greenford, Middlesex UB6 0HE, England **Effects of capsaicin on nociceptive heat, pressure and chemical thresholds and on substance P levels in the rat.** *Brain Research*. 189(2):561-564, 1980.

The effects of systemically applied capsaicin on nociceptive response evoked by heat, chemical, and pressure stimuli were compared with substance-P (SP) levels in spinal cord and skin. Groups of 30 rats were injected s.c. daily with increasing doses of capsaicin or vehicle for 5 days, and nociceptive thresholds were determined on the fifth day after the last injection and at 14 day intervals thereafter up to 68 days. SP content of the ventral and dorsal horns of the cervical spinal cord and of skin taken from the hind paw was determined on day 21. Results indicate that capsaicin markedly elevated nociceptive chemical and pressure thresholds, but had no effect or even slightly re-

duced nociceptive heat thresholds. The associated depletion of SP from dorsal horn and skin indicates that SP is most likely to mediate transmission of pressure and chemically-induced nociception at primary afferent terminals, but it is unlikely to be the neurotransmitter for heat-induced nociception. This infers that heat and nonheat nociception are subserved by different, but probably converging, anatomical pathways. 10 references.

001284 Hefti, Franz; Melamed, Eldad; Sahakian, Barbara J.; Wurtman, Richard J. Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Circling behavior in rats with partial, unilateral nigro-striatal lesions: effect of amphetamine, apomorphine, and DOPA.** *Pharmacology Biochemistry and Behavior*. 12(2):185-188, 1980.

Partial, unilateral lesions of the nigrostriatal tract were produced in rats by injecting various quantities of 6-hydroxydopamine into the substantia nigra and the extent of each animal's lesion was estimated by comparing tyrosine hydroxylase activity in its lesioned and control striata. L-DOPA and apomorphine-induced contralateral (i.e., away from the lesion) circling behavior only in rats in which more than 90% of the nigrostriatal system had been destroyed. In contrast, d-amphetamine caused turning in the ipsilateral direction when as few as 50% of the nigrostriatal neurons had been destroyed. It is concluded that rats with partial, unilateral nigrostriatal lesions of varying severity might be good experimental models for moderate forms of Parkinson's disease. 18 references. (Author abstract modified)

001285 Helke, C. J.; O'Donohue, T. L.; Jacobowitz, D. M. Laboratory of Clinical Science, Bldg. 10, NIMH, Bethesda, MD 20205 **Substance P as a baro- and chemoreceptor afferent neurotransmitter: immunocytochemical and neurochemical evidence in the rat.** (Unpublished paper). Bethesda, MD, NIMH, 1980. 21 p.

The contribution of vagal afferent input to the substance-P (SP) content of the nucleus tractus solitarius (NTS) in the rat was assessed, immunocytochemistry was used to visualize SP immunoreactivity (SP-I) in peripheral baroreceptive and chemoreceptive regions in the rat, and the SP immunoreactive material in the hindbrain was characterized with high pressure liquid chromatography. It was found that the NTS contained significant amounts of SP-I and that unilateral removal of the nodose ganglia reduces the SP-I content of those portions of the NTS known to receive vagal afferents. In addition, SP-I was visualized in discrete fibers in the tunica adventitia of the aortic arch and carotid sinus regions, the vagus nerve, and nodose ganglia. These results in the rat are consistent with previous studies in the cat and provide further evidence that SP is contained within baroreceptor and chemoreceptor afferent nerves. 22 references. (Author abstract modified)

001286 Hevor, T.; Gayet, J. Laboratoire de Physiologie Generale, Universite de Nancy 1, C. O. 140, F-54037 Nancy, France **Effect of methionine sulfoximine on brain cyclic nucleotide levels.** *Neuropharmacology*. 18(12):1029-1031, 1979.

The effects of methionine sulfoximine or regional levels of brain cyclic AMP and cyclic GMP were examined in male Swiss mice and Wistar rats. Animals were sacrificed during the preconvulsive, convulsive, and postconvulsive periods or 4, 8, and 24 hours, respectively, after i.p. injection of 100mg/kg L-methionine-DL-sulfoximine. Cyclic AMP contents in the brain regions examined were not significantly altered, cyclic GMP was significantly increased in the brainstem and cerebral cortex during the seizure period and in the brainstem during the post-convulsive recovery period. It is suggested that methionine sulfoximine or its metabolites exerts a stimulating effect on specif-

ic neuronal cells in the brainstem, which is followed by an induction of gluconeogenesis in glial cells. 14 references.

001287 Hevor, Tobias K.; Gayet, Jacques. Laboratoire de Physiologie Generale, Faculte des Sciences, Universite de Nancy 1, F-54037 Nancy, France **Cyclic nucleotides in the brain of mice and rats submitted to the convulsant, methionine sulfoximine**. *Biochemical Pharmacology*. 28(24):3507-3512, 1979.

Regional cAMP and cGMP levels were measured in the rat and mouse brain following i.p. injection of the convulsant methionine sulfoximine (MSO) at a dose of 100mg/kg. No change in cAMP content was noticeable in mouse cerebral cortex or in rat cerebral cortex, striatum, hypothalamus, and cerebellum during the preconvulsive and postconvulsive periods. cGMP content increased in mouse cerebral cortex and brainstem, but did not change in cerebellum during the period of MSO-induced seizure activity. At the time of recovery from seizures, the increase in cGMP persisted only in brainstem. During the whole preconvulsive period, cGMP level rose in the brainstem. At 50mg/kg, MSO induced a relatively decreased increase of cGMP in brainstem only. It is suggested that the increase in cGMP level may develop simultaneously in neuronal and glial cells, primarily in brainstem, during some periods following MSO administration. 25 references. (Author abstract modified)

001288 Heydorn, William; Frazer, Alan; Mendels, Joe. Veterans Administration Hospital, University and Woodland Aves., Philadelphia, PA 19104 **Do tricyclic antidepressants enhance adrenergic transmission? An update**. *American Journal of Psychiatry*. 137(1):113-114, 1980.

The effects of single and repeated administration of desmethylimipramine (DMI) on a response that is elicited by norepinephrine (NE) released endogenously from sympathetic nerves was investigated by examining the pineal gland of the rat. The animals were given either a single injection of DMI or nine injections over a 5 day period. Changes in the activity of the sympathetic nerve to the pineal were manipulated by moving animals that have been kept in the light into the dark. The results demonstrate that while acute administration of DMI enhance a response elicited by endogenously released NE, repeated administration of the tricyclic blocked noradrenergic responsiveness. The findings demonstrate that the effects of chronic administration of DMI are opposite to those found after a single injection of the antidepressant. 10 references.

001289 Hirata, Fusao; Schiffmann, Elliot; Venkatasubramanian, Krishnamoorthy; Salomon, David; Axelrod, Julius. Section on Pharmacology, Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **A phospholipase A2 inhibitory protein in rabbit neutrophils induced by glucocorticoids**. (Unpublished paper). Bethesda, MD, NIMH. 1980. 18 p.

The existence of a protein in rabbit neutrophils that inhibits phospholipase A2 and whose synthesis is induced by glucocorticoids is reported. When rabbit peritoneal neutrophils were treated with glucocorticoids, their chemotactic response to stimulation by the chemoattractant, fMet-Leu-Phe, was markedly reduced. Preincubation of cells with glucocorticoids also decreased phospholipase A2 activity in situ as measured by the release of (1-14C) arachidonic acid previously incorporated into phospholipids. The inhibitory potencies of glucocorticoids on phospholipase A2 activity correlated well with their anti-inflammatory activities and their abilities to bind to glucocorticoid receptors. Inhibitors of RNA and protein synthesis suppressed the inhibitory effect of glucocorticoids on phospholipase A2 activity. Digestion of the glucocorticoid treated cells by pronase overcame the inhibitory activity. Phospholipase A2 activity induced by Ca²⁺ ionophore, A23187, was not affected by pronase

treatment. Gel filtration of proteins from neutrophil membranes labelled with (3H) lysine showed an induction of protein(s) after glucocorticoid treatment. This protein inhibited a partially purified pancreatic phospholipase A2 and reduced the peptide initiated chemotactic response of neutrophils. 19 references. (Author abstract modified)

001290 Hirata, Fusao; Tallman, John F.; Henneberry, Richard C.; Mallorga, Pierre; Strittmatter, Warren J.; Axelrod, Julius. Section on Pharmacology, Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Phospholipid methylation: a possible mechanism of signal transduction across biomembranes**. (Unpublished paper). Bethesda, MD, NIMH. 1980. 11 p.

Several lines of evidence are presented which suggest that the turnover of phospholipids, especially methylated phospholipids, is involved in the regulation of the beta-adrenergic receptor/adenylate cyclase system in HeLa cells, C6 astrocytoma cells, lymphocytes, mast cells, and reticulocytes. The conversion of phosphatidylethanolamine to phosphatidylcholine is catalyzed by two methyltransferases with S-adenosylmethionine as the methyl donor. Phosphatidylcholine formed by transmethylation is further metabolized by phospholipase A2. The synthesis and degradation of methylated phospholipids are involved in regulating the number of the beta-adrenergic receptors and their coupling to adenylyl cyclase in rat reticulocytes, HeLa cells, and rat astrocytoma cells. Methylation of the phospholipids in these cells is stimulated by binding of agonists to the beta-adrenergic receptors. Accumulation of phosphatidyl-N-monomethylethanolamine causes an increase in membrane fluidity and enhances the coupling of the receptors to adenylyl cyclase. Agents that inhibit phospholipid methylation decrease the number of receptors in intact HeLa cells, while increased phospholipid methylation unmasks cryptic receptors. Conversely, the degradation of methylated phospholipids appears to be closely associated with the desensitization of the beta-adrenergic receptors following prolonged stimulation with isoproterenol. Inhibition and stimulation of phospholipase A2 causes inhibition and stimulation of the desensitization process. 19 references. (Author abstract modified)

001291 Hockel, S. H. J.; Muller, W. E.; Wollert, U. Pharmakologisches Institut der Universität Mainz, Obere Zahlbacher Strasse 67, D-6500 Mainz, Germany **Diazepam increases L-tryptophan uptake into various regions of the rat brain**. *Research Communications in Psychology, Psychiatry and Behavior*. 4(4):467-475, 1979.

The relationship between diazepam and L-tryptophan uptake into the brain was investigated. The uptake of L-tryptophan into slices of six regions of the rat brain (cortex, striatum, hippocampus, hypothalamus, midbrain, cerebellum) was significantly increased by diazepam. Diazepam increased the Vmax of the L-tryptophan uptake system, while its Km was nearly unchanged. The half maximal effect of diazepam was observed at about 100mM diazepam in the incubation medium. 14 references. (Author abstract modified)

001292 Hoffman, Andrew R.; Paul, Steven M.; Axelrod, Julius. Section on Pharmacology, Laboratory of Clinical Science, NIMH, Bldg. 10, Rm. 2047, Bethesda, MD 20205 **The enzymatic formation of catecholestrogens from 2-methoxyestrogens by rat liver microsomes**. (Unpublished paper). Bethesda, MD, NIMH. 1979. 24 p.

A sensitive and specific radioenzymatic assay for rat liver 2-methoxyestrogen demethylase has been developed which makes it possible to characterize its substrate requirements and to study the influence of various hormones on catecholesteron formation. It was found that 2-methoxyestrogen demethylase activity

is located in rat liver microsomes. The apparent K_m for 2-methoxyestrone (2MeOE1) is 12 μM and for 2-methoxyestradiol (2MeOE2), 3 μM . The two most prevalent 2-methoxyestrogens, 2MeOE1 and 2MeOE2, appear to be demethylated by different enzymes. The enzymes have an absolute requirement for NADPH, and their activities are inhibited by CO and SKF-525A, indicating that they are cytochrome P450 dependent. 2MeOE2 demethylation but not 2MeOE1 demethylation exhibits substrate inhibition. 2MeOE1 demethylase activity in the female rat liver is only one third that of the male, but sexual dimorphism was not found in 2MeOE2 demethylation. Thyroidectomy and estradiol treatment of the male rat resulted in diminished 2MeOE1 but not 2MeOE2 demethylation. 28 references. (Author abstract modified)

001293 Holbrook, Larry Albert. University of Toronto (Canada) **Transient decrease in brain protein synthesis after in vivo administration of a psychotropic drug: mechanism and developmental effects.** (Ph.D. dissertation). Dissertation Abstracts International. 39(7):3106-B, 1979. (Not available from Univ. Microfilms), 1977.

The effect of intravenous injection of LSD on the translational apparatus of rabbit brain was examined. It was discovered that brain polysomes were disaggregated after in vivo administration of this psychotropic agent. Characteristics of this poly-some response in brain to LSD were then analyzed. A profound effect of LSD on brain protein synthesis is noted. The important role of synaptic activity mediating regulatory aspects of macromolecular metabolism in brain is suggested. The degree of effect appears to be related to the amount of stress on the animal, a significant aspect to consider in the therapeutic as well as abusive usage of such a psychoactive drug. It is reported that the effects of receptor binding agents further verified recent suggestions that LSD may act on serotonin and dopamine receptors. (Journal abstract modified)

001294 Hong, J. S.; Wood, P. L.; Gillin, J. C.; Yang, H.-Y. T.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Recurrent convulsions and hippocampal (met5)-enkephalin content.** (Unpublished paper). Washington, DC. NIMH, 1980. 13 p.

The relationship between convulsions and the content of hippocampal (met5)-enkephalin (ME) was studied through the effects of convulsions induced by intracerebral injections of kainic acid (KA) or ioniazid or by electroconvulsive shocks (ECS) on the ME content of rat hippocampus. The data demonstrate that the metabolic state of ME stored in hippocampal neurons can change in response to recurrent seizures. A decrease in the hippocampal content of ME is elicited at 6 hours after the intrahippocampal injection of KA. Since during this period the rats exhibit recurrent seizures it can be inferred that these seizures increase the utilization of hippocampal ME. This inference is supported by several findings indicating that hippocampal neurons usually participate in convulsive states of different origin. Following the initial decrease, the hippocampal content of ME rises and is maintained at a level higher than normal for a long period of time. This persistent increase may reflect an activation of a rate limiting process important in the regulation of the biosynthesis of this pentapeptide. As a consequence of this activation, the steady state concentration of hippocampal ME increases. The increases in hippocampal ME content can be prevented by pretreatment with anticonvulsants. The hippocampal ME content can be increased by repeated ECS or by injections of ioniazid at doses which cause recurrent convulsions. 18 references.

001295 Hood, William F.; Harris, R. Adron. Dept. of Pharmacology, University of Missouri School of Medicine, Columbia,

MO 65212 **Effects of pentobarbital, ethanol and morphine on subcellular localization of calcium and magnesium in brain.** Biochemical Pharmacology. 28(20):3075-3080, 1979.

The calcium and magnesium content of brain tissue and subcellular fractions were examined after acute and chronic treatment with morphine, ethanol, and pentobarbital and after chronic treatment with ethanol and pentobarbital. Acute administration of pentobarbital to male Swiss-Webster mice significantly decreased the calcium content of synaptic plasma membranes (SPM), but increased the calcium content of extrasynaptosomal mitochondria; the calcium content of the SPM remained depressed with chronic pentobarbital, but no further changes were detected. Pentobarbital did not alter the subcellular localization of magnesium in brain. Acute injection of morphine decreased the synaptosomal calcium concentration in male Sprague-Dawley rat brain, but acute ethanol treatment had no effect on the calcium content of any subcellular fraction studied. Acute treatment with ethanol or morphine also failed to alter the calcium or magnesium content of tissue samples from rat cortex. Chronic ethanol treatment did not alter the concentration of calcium in any subcellular fraction, but did decrease the concentration of magnesium in myelin and serum. The role of magnesium deficiency in chronic alcoholism is discussed. 27 references. (Author abstract modified)

001296 Hood, William F.; Harris, R. Adron. Dept. of Pharmacology, University of Missouri School of Medicine, Columbia, MO 65212 **Effects of depressant drugs and sulphydryl reagents on the transport of calcium by isolated nerve endings.** Biochemical Pharmacology. 29(6):957-959, 1980.

The effects of sulphydryl reagents and depressant drugs known to inhibit the transport of calcium by sarcoplasmic reticulum, were studied on ATP-dependent calcium transport by lysed rat synaptosomes. The results showed that depressants such as ethanol, pentobarbital, and acetaldehyde significantly inhibited the ATP dependent uptake, while chlorpromazine, diphenylhydantoin, and phenylcyclidine were without effect. In contrast, the potassium stimulated uptake was inhibited by pentobarbital, chlorpromazine, diphenylhydantoin, ethanol, phenylcyclidine, and acetaldehyde. With all the depressant drugs, the inhibition of the potassium stimulated uptake was much greater than that seen with the ATP dependent uptake. The sulphydryl reagents inhibited intrasynaptosomal ATP dependent calcium uptake more strongly than they inhibited potassium stimulated uptake. Inhibition of ATP dependent uptake may account for the increase in spontaneous release of neurotransmitters that has been observed with sulphydryl reagents and with high concentrations of depressants and anesthetics. Alternative arguments are also presented. 36 references.

001297 Horn, Alan S.; Kelly, Peter; Westerink, Ben H. C.; Dijkstra, Durk. Dept. of Pharmacy, University of Groningen, 2 Antonius Deusinglaan, Groningen, The Netherlands **A prodrug of ADTN: selectivity of dopaminergic action and brain levels of ADTN.** European Journal of Pharmacology. 60(1):95-99, 1979.

The effects of a prodrug of 2-amino-6,7-dihydroxytetrahydronaphthalene (ADTN), dibenzoyl ADTN, on ADTN concentrations in male Sprague-Dawley rat brain and on the behavior of rats with unilateral 6-hydroxydopamine lesions in the corpus striatum were studied. A high pressure liquid chromatography/electrochemical detection assay revealed a more selective accumulation of ADTN in the corpus striatum than in the cerebellum; the accumulation of ADTN in the corpus striatum was slow in onset and long in duration. The concentration of ADTN in the striatum appeared to be high enough to significantly stimulate presynaptic dopamine receptors, but not to stimulate supersensitive postsynaptic dopamine

receptors involved in rotational behavior. 11 references. (Author abstract modified)

001298 Hotchkiss, Adair J.; Morgan, Michael E.; Gibb, James W. Dept. of Biochemical Pharmacology and Toxicology, University of Utah, Salt Lake City, UT 84112 **The long-term effects of multiple doses of methamphetamine on neostriatal tryptophan hydroxylase, tyrosine hydroxylase, choline acetyltransferase and glutamate decarboxylase activities.** *Life Sciences*. 25(16):1373-1378, 1979.

The long-term effects of methamphetamine (15mg/kg) on neostriatal enzyme activity were measured in male Sprague-Dawley rats treated every 6 hours for 24 hours and subsequently monitored for up to 30 days. Tyrosine hydroxylase was maximally decreased the first day after drug treatment, but the depression persisted through the 30 day observation period. Tryptophan hydroxylase was depressed to 17% of control within 15 hours of the first injection and remained maximally depressed 7.5 days after the last dose of the drug. Neostriatal choline acetyltransferase and glutamate decarboxylase activities were not altered acutely or chronically by methamphetamine treatment. Results suggest that the reported neurotoxic effects of methamphetamine are due to selective alteration of dopaminergic and serotonergic neurons rather than to generalized destruction of the neostriatum. 17 references. (Author abstract modified)

001299 Howlett, D. R.; Nahorski, S. R. Dept. of Pharmacology and Therapeutics, Medical Sciences Building, University of Leicester, University Road, Leicester, LE1 7RH, England **Quantitative assessment of heterogeneous 3H-spiroperone binding to rat neostriatum and frontal cortex.** *Life Sciences*. 26(7):511-517, 1980.

Anomalies of the binding of 3H-spiroperone to rat cerebral membranes were examined. By employing a very low ligand concentration it is demonstrated that even within the corpus striatum, 3H-spiroperone appears to bind multiple sites and that dopaminergic and serotonergic agents can selectively inhibit from these sites. In the corpus striatum, 75% to 85% of the 3H-spiroperone specific binding can be inhibited with high affinity by dopaminergic drugs while some 20% to 30% is inhibited with high affinity by serotonergic compounds. The two 3H-spiroperone sites, which have been shown to have affinities of 31 and 325pM, may therefore represent dopaminergic and serotonergic sites. At higher concentrations of 3H-spiroperone, however, the picture may be complicated by a further low affinity site. The great selectivity shown by dopaminergic agonists for the two 3H-spiroperone sites explains the flattened displacement curves reported for 3H-spiroperone/agonist interactions. As dopaminergic agents show the greater affinity for the high affinity 3H-spiroperone site, it is tempting to speculate that this site has the greatest association with the dopamine receptor. 25 references. (Author abstract)

001300 Hrdina, P. D.; Elson, K. Dept. of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada K1N 9A9 **High-affinity choline uptake in regions of rat brain and the effect of antidepressants.** *Canadian Journal of Physiology and Pharmacology*. 57(6):595-599, 1979.

The effect of tricyclic antidepressants, chlorpromazine, and some monoamine oxidase inhibitors on the accumulation of (14C) choline by crude synaptosomal (P2) fraction from different regions of rat brain (cortex, striatum, and hippocampus) was investigated. Analysis of choline uptake kinetics resulted in high and low affinity components with different Michaelis constants. All tricyclic antidepressants tested inhibited in a dose dependent manner the high affinity choline uptake in the 3 regions, amitriptyline being the most potent. The IC50 values correlated sig-

nificantly with the relative potencies of imipramine congeners in binding to muscarinic receptors in the brain. Neither tranlycypromine nor pargyline in concentrations up to 0.1mM had any effect on choline transport. Concentrations of tricyclic antidepressants effective in inhibiting the uptake of choline failed to influence significantly in activity of choline acetyltransferase in brain regions examined. The results suggest that the effect of imipramine congeners on high affinity choline uptake may be reflected in the anticholinergic properties of these compounds. 20 references. (Author abstract)

001301 Hunt, Peter; Raynaud, Jean-Pierre; Leven, Margret; Schacht, Ulrich. Centre de Recherches Roussel Uclaf, F-93230 Romainville, France **Dopamine uptake inhibitors and releasing agents differentiated by the use of synaptosomes and field-stimulated brain slices in vitro.** *Biochemical Pharmacology*. 28(13):2011-2016, 1979.

The dopamine (DA) uptake inhibitory and releasing properties of the antidepressant nomifensine, the psychostimulants amphetamine and methylphenidate, and the antiparkinson agent benzotropine were examined in rat brain striatal synaptosomes and slices. High concentrations of nomifensine and amphetamine caused increases in the amount of radioactivity in the medium when they were incubated with synaptosomes preloaded with (3H)DA, but the two drugs appeared to act by different mechanisms since their effects were not additive. When reuptake of DA was minimized, amphetamine showed a strong releasing effect, but nomifensine, benzotropine, and methylphenidate were inactive. Methylphenidate and amphetamine both increased the overflow of radioactivity in preloaded, electrically stimulated striatal slices. Results suggest that nomifensine and benzotropine are pure uptake inhibitors, whereas amphetamine and methylphenidate are releasing agents. 25 references. (Author abstract modified)

001302 Hutson, P. H.; Knott, P. J.; Curzon, G. Dept. of Neurochemistry, Institute of Neurology, 33 John's Mews, London WC1N 1NS, England **Effect of isoprenaline infusion on the distribution of tryptophan, tyrosine and isoleucine between brain and other tissues.** *Biochemical Pharmacology*. 29(4):509-516, 1980.

Intravenous infusion of anesthetized rats with the beta-adrenoreceptor agonist isoprenaline decreased plasma total tryptophan concentration and increased both plasma free and brain tryptophan concentrations. Muscle tryptophan and also concentrations showed moderate significant decreases, but concentrations in liver and kidney did not alter significantly. Plasma tyrosine concentration fell and brain tyrosine concentration rose, but these changes were less marked than those of tryptophan. Isoprenaline infusion considerably increased egress of 14C-tryptophan from plasma and moderately increased egress of 14C-isoleucine, but did not alter egress of 14C tyrosine. However, 5 minutes after pulse injection of any of the above 14C labelled amino acids, the isoprenaline infused rats had higher brain counts than control animals. Results are consistent with previous evidence that increased availability of tryptophan to the brain can occur in stressful situations. 23 references. (Author abstract)

001303 Hyttel, J.; Nielsen, I. Moller, Dept. of Pharmacology and Toxicology, H. Lundbeck and Co. A/S, DK-2500 Valby, Denmark **Tardive dyskinesia and dopamine receptors.** *Lancet*. No. 8155:1300, 1979.

The effects of a large series of neuroleptics on binding of 3H-haloperidol and 3H-cis (Z)-flupenthixol and on dopamine stimulated adenylate cyclase were examined. It was found that results in the latter two tests correlated closely, whereas effects in 3H-haloperidol binding deviated distinctly from them. Calculating the ratios between effects in 3H-haloperidol binding and the

latter two tests to obtain a measure of the selectivity of neuroleptics with respect to D1 and D2 binding indicated no selective antagonists of D1 among the 42 tested neuroleptics. Thus, specific D1 receptor antagonists have not been found, and among the proposed selective D2 antagonists, some are known to induce tardive dyskinesia. Others may be less likely to cause these unwanted effects, but clinical experience does not yet seem sufficient to substantiate such a claim. 5 references.

001304 Hyttel, John. Dept. of Pharmacology and Toxicology, H. Lundbeck and Co. A. S. Ottiliavej 7-9, DK-2500 Copenhagen-Valby, Denmark. **Further evidence that 3H-Cis(Z)flupenthixol binds to the adenylate cyclase-associated dopamine receptor (D-1) in rat corpus striatum.** *Psychopharmacology*. 67(1):107-109, 1980.

The proposal that 3H-cis(Z)flupenthixol (3H-FPT) preferentially binds to striatal dopamine receptors associated with adenylate cyclase activity (D-1), distinct from dopamine receptors which 3H-haloperidol (3H-hal) binds (D-2), was investigated. The dopamine agonists bromocriptine and ergotamine were 60 times more potent as displacers of 3H-hal than 3H-FPT binding. Other dopamine agonists (ergometrine, dopamine, apomorphine, 2-amino-6,7-dihydroxytetralin (ADTN), and ertocornine) also shared this profile, although a smaller ration was found for these compounds. Substituted benzamides (clebopride greater than siltopride greater than sulpiride greater than metoclopramide greater than tiapride) displace 3H-hal but have only a very slight displacing effect towards 3H-FPT, and did not inhibit dopamine stimulated adenylate cyclase activity. The same pattern is shared by oxiperomide and molindone. Together, these results support the idea that 3H-FPT labels another class of dopamine receptors than does 3H-hal, and that the former class most likely is associated with adenylate cyclase. 12 references. (Author abstract)

001305 Iadarola, Michael J.; Gale, Karen. Gale: Georgetown University, Dept. of Pharmacology, 3900 Reservoir Road, Washington, DC 20007. **Dissociation between drug-induced increases in nerve terminal and non-nerve terminal pools of GABA in vivo.** *European Journal of Pharmacology*. 59(1/2):125-129, 1979.

The effects of n-dipropylacetate (DPA) and amino-oxyacetic acid (AOAA) on the GABA content of the substantia nigra (SN) were determined in intact male Sprague-Dawley rats and in rats in which the GABA containing afferent projections to the SN had been unilaterally destroyed. AOAA and DPA produced similar increases in GABA content in the SN of the intact rats. In the GABA denervated rats, however, AOAA (30mg/kg) doubled the GABA content in the SN, but DPA (300mg/kg) had no effect. Results suggest that the GABA increase produced by DPA is associated with GABA containing nerve terminals, while that produced by AOAA is associated primarily with nonnerve terminal components (neural perikarya and glial cells) that were not destroyed by the lesions. 11 references. (Author abstract modified)

001306 Ide, Haya; Nakazawa, Yasuo. Medical Research Institute, Tokyo Medical and Dental University, 3-10, 2-chome, Kanda-Surugadai, Chiyoda-ku, Tokyo 101, Japan. **Effect of chlorpromazine on the cytoplasmic phosphatidate phosphohydrolase in rat liver.** *Biochemical Pharmacology*. 29(5):789-793, 1980.

The inhibitory effect of chlorpromazine on phosphatidate phosphohydrolase activity was studied with respect to the selectivity of the molecular species of phosphatidate. Rat liver microsomes which include endogenously labeled (14C)phosphatidic acid were prepared by the incubation of microsomes with sn(14C)glycerol-2-phosphate and used as substrate. The distribu-

tion of radioactivity among the molecular species of (14C)phosphatidate remaining after incomplete hydrolysis of the substrate exhibited little difference from that of the untreated substrate. When the hydrolysis was suppressed by the addition of chlorpromazine, however, the radioactivity distributed in the monoenoic and dienoic (14C)phosphatidate increased. The preference of the molecular species of phosphatidate in the inhibition was further confirmed by the experiment run with microsomes containing 2-(1-14C)palmitoyl, oleoyl, linoleoyl and arachidonyl species of phosphatidate as substrate. 24 references. (Author abstract)

001307 Ieiri, T.; Chen, H. T.; Meites, J. Meites: Dept. of Physiology, Michigan State University, East Lansing, MI 48824. **Naloxone stimulation of luteinizing hormone release in prepubertal female rats; role of serotonergic system.** *Life Sciences*. 26(15):1269-1274, 1980.

Whether naloxone stimulated luteinizing hormone (LH) release via a serotonergic mechanism, was studied in rats. Injection of naloxone hydrochloride into 25-day-old female prepubertal rats resulted in a significant elevation in serum LH 30 minutes later. Injection of this same dose of naloxone together with morphine sulfate resulted in inhibition of naloxone-induced LH release. When rats were first injected with 5-hydroxytryptophan (5-HTP) to increase hypothalamic serotonin content, naloxone failed to increase serum LH levels. On the other hand, when parachlorophenylalanine (PCPA) was given first to reduce hypothalamic serotonin content, naloxone-induced LH release was potentiated. Morphine failed to inhibit the naloxone-induced rise in serum LH when PCPA was first administered. Neither 5-HTP nor PCPA, when injected alone, altered serum LH values. Results suggest that naloxone promotes LH release by reducing hypothalamic serotonergic activity, and morphine inhibits LH release by increasing hypothalamic serotonergic activity. 14 references. (Author abstract modified)

001308 Ishizaka, Teruko; Hirata, Fusao; Ishizaka, Kimishige; Axelrod, Julius. Johns Hopkins University School of Medicine at the Good Samaritan Hospital, Baltimore, MD 21239. **Stimulation of phospholipid methylation, Ca²⁺ influx and histamine release by bridging of IgE receptors on rat mast cells.** (Unpublished paper). Bethesda, MD, NIMH, 1980. 20 p.

Normal rat mast cells were stimulated by antibodies against IgE receptors (anti-RBL) or by anti-IgE, and 3H-methyl group incorporated into phospholipids, 45Ca uptake, and histamine release was examined. Anti-RBL or its F(ab')₂ fragments as well as anti-IgE induced an increase in the incorporation of 3H-methyl group into phospholipids, 45Ca influx, and histamine release. By contrast, Fab' monomer fragments of anti-RBL induced none of these reactions. The transient increase of 3H-methyl group incorporation in lipids peaked within 15 seconds after the addition of either anti-RBL or anti-IgE, and fell to basal level in 30 seconds. This was then followed by an influx of 45Ca rising to a maximum in 2 minutes and by histamine release which reached a maximum in 3 minutes. Inhibition of phospholipid methylation resulted in an inhibition of 45Ca influx and histamine release. These findings demonstrate that phospholipid methylation in rat mast cells is induced by bridging of IgE receptors on the cell surface and that increased methylation of phospholipids sets the stage for an influx of Ca²⁺ and subsequent release of histamine. 18 references. (Author abstract)

001309 Iversen, L. L.; Iversen, S. D.; Bloom, F. E. A. V. Davis Center for Behavioural Neurobiology, Salk Institute, La Jolla, CA 92037. **Opiate receptors influence vasopressin release from nerve terminals in rat neurohypophysis.** *Nature*. 284(5754):350-351, 1980.

The hypothesis that enkephalin innervation of the pars nervosa originating from the magnocellular hypothalamic nuclei regulates the secretion of neurohypophyseal hormones was investigated. The finding that a stable enkephalin analogue (D-Ala²,D-Leu⁵-enkephalin) inhibits the calcium dependent release of vasopressin evoked by electrical stimulation of the rat pituitary stalk *in vitro* is reported as support for the hypothesis. A similar inhibition of the stimulus evoked vasopressin release is caused by morphine and beta-endorphin, and the inhibitory effects of the enkephalin analogue can be reversed by naloxone. These findings suggest the possible existence of inhibitory opiate receptors on the terminals of vasopressin fibers in the pars nervosa. 19 references. (Author abstract modified)

001310 Jacob, Peyton, III; Kline, Toni; Castagnoli, Neal, Jr. Castagnoli: Dept. of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, CA 94143 **Chemical and biological studies of 1-(2,5-dihydroxy-4-methylphenyl)-2-aminopropane, an analogue of 6-hydroxydopamine.** Journal of Medicinal Chemistry. 22(6):662-671, 1979.

The chemical and biological properties of the bis(O-demethyl)-p-hydroquinone metabolite of the psychotomimetic amine 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) were determined. The quinone and imino quinone intermediates resulting from the oxidation of the hydroquinone metabolite were characterized, and the interactions of these intermediates with nucleophilic reagents and with biological macromolecules were examined. Since the properties of the hydroquinone metabolite parallel those reported for the structurally related sympatholytic compound 6-hydroxydopamine, it is hypothesized that the psychotomimetic properties of DOM may be mediated through 6-hydroxydopamine type interactions of the hydroquinone with important macromolecules in the brain. 28 references. (Author abstract modified)

001311 Jacoby, J. H.; Thomas, R. F.; Poulakos, J. J.; Siegel, A. Siegel: New Jersey Medical School, College of Medicine and Dentistry of New Jersey, 100 Bergen St., Newark, NJ 07103 **Studies on tryptophan accumulation in brain during methiothepin-induced enhancement of 5-hydroxyindole synthesis.** Naunyn-Schmiedeberg's Archives of Pharmacology. 307(2):143-149, 1979.

Pretreatment with the serotonin receptor antagonist methiothepin potentiated the elevation of brain tryptophan, 5-hydroxytryptophan, and 5-hydroxyindoles (serotonin and 5-hydroxyindoleacetic acid) induced by tryptophan loading in male Sprague-Dawley rats. Coadministration of valine with tryptophan attenuated these effects even in rats pretreated with methiothepin. After administration of methiothepin and tryptophan to rats with widespread reduction of brain 5-hydroxyindole levels resulting from raphe lesions of 5,7-dihydroxytryptamine brain tryptophan levels rose considerably above the sum of the increases found in animals given one or the other. In rats with transected spinal cords, enhanced tryptophan uptake and 5-hydroxyindole synthesis after methiothepin and tryptophan treatment was observed in the cranial portion but not in the caudal segment. Results suggest that even though enhanced tryptophan uptake can occur in the presence of minimal neuronal activity, 5-hydroxyindole synthesis and tryptophan uptake are impaired when nerve impulse flow is eliminated. 28 references. (Author abstract modified)

001312 Jakoubek, Bohumil; Hajek, Ivan; Buresova, Milena. Institute of Physiology, Czechoslovak Academy of Sciences, Videnka 1083, 14220 Prague 4, Czechoslovakia **Different effects of chlorpromazine on the synthesis of proteins in cell-free systems of rat cortex, hippocampus, medulla and cerebellum.** Brain Research. 182(1):242-245, 1980.

The capacity of ribosomes prepared from Sprague-Dawley rat cerebellum, medulla, hippocampus, and cortex to synthesize proteins was determined 1, 2, and 4 hours after *in vivo* administration of chlorpromazine (5mg/kg i.p.). Protein synthesis was markedly decreased in cerebellum and medulla 1 to 2 hours after chlorpromazine administration. In hippocampus, protein synthesis was increased 1 hour and decreased 2 hours after chlorpromazine. No changes were found in cortex at 1 or 2 hours. Protein synthesis was increased in all four regions 4 hours after chlorpromazine. It is suggested that chlorpromazine interferes with the synthesis of messenger RNA. 11 references.

001313 Johansson, Barbro B.; Martinsson, Lena. Dept. of Neurology, University of Goteborg, Sahlgren Hospital, Goteborg, Sweden **Beta-adrenoreceptor antagonists and the dysfunction of the blood-brain barrier induced by adrenaline.** Brain Research. 181(1):219-222, 1980.

In a study of the effects of hypertension on the permeability of the blood-brain barrier, male Sprague-Dawley rats were pretreated with various beta-adrenoreceptor antagonists prior to *i.v.* infusion of adrenaline. The leakage of albumin into the brain was significantly decreased by pretreatment with D,L-propranolol, but not D-propranolol. Albumin leakage was diminished after metoprolol, but not after butoxamine. Results suggest that the decrease in albumin leakage after D,L-propranolol was caused by inhibition of beta-adrenoreceptors. 14 references.

001314 Johnson, Richard W.; Yamamura, Henry I. Dept. of Biochemistry, College of Medicine, University of Arizona Health Sciences Center, Tucson, AZ 85724 **Photoaffinity labeling of the benzodiazepine receptor in bovine cerebral cortex.** Life Sciences. 25(18):1613-1620, 1979.

Clonazepam, nitrazepam, and flunitrazepam interacted irreversibly with benzodiazepine binding sites in bovine cerebral cortex homogenates irradiated with ultraviolet light. Photoaffinity labeling with (3H)flunitrazepam was reduced by about 85% by several benzodiazepines, including clonazepam, lorazepam, and unlabeled flunitrazepam. Spiroperidol, atropine, naltrexone, propranolol, and GABA had no effect on irreversible (3H)flunitrazepam binding. 9 references. (Author abstract modified)

001315 Jones, D. L.; Veale, W. L.; Cooper, K. E. Faculty of Medicine, Dept. of Physiology, University of Western Ontario, London, Ontario N6A 5C1, Canada **Alterations in body temperature elicited by intrahypothalamic administration of tetrodotoxin, ouabain and A23187 ionophore in the conscious cat.** Brain Research Bulletin. 5(1):75-80, 1980.

Ouabain, tetrodotoxin, and calcium selective ionophore (A23187) were administered bilaterally into the hypothalamus of the unrestrained, fully conscious cat, while body temperature and other indicators of thermoregulatory responses were monitored continuously. Posterior hypothalamic microinjection of 2.0 to 10.0ng or tissue perfusion with ouabain elicited dose dependent increases in body temperature accompanied by pinnae vasoconstriction, shivering and postural changes consistent with heat conservation. Tetrodotoxin, microinjected in doses of 0.5 and 5.0ng or tissue perfusions in the posterior hypothalamus elicited dose dependent falls in body temperature. However, tetrodotoxin microinjected into the anterior hypothalamic region elicited only increases in temperature. The calcium selective ionophore A23187, at least at the concentrations used in this study, did not appear to produce any consistent effects on thermoregulation. These data support the hypothesis that the ionic milieu of the posterior hypothalamic region is essential in the maintenance of body temperature. Further, they suggest that increasing the ratio of calcium to sodium acts in a manner similar

to a depression in the firing frequency of a distinct population of cells, which may in turn determine in some way the set point for body temperature. There is no evidence to support the concept that increasing the ratio of calcium to sodium causes an increased release of the synaptic contents of the region. 41 references. (Author abstract modified)

001316 Jori, A.; Caccia, S.; Guiso, A.; Ballabio, M.; Garattini, S. Istituto di Ricerche Farmacologiche, Mario Negri Via Eritrea, 62.I-20157 Milan, Italy **Selective storage of p-hydroxy-d-amphetamine in the dopaminergic nerve terminals**, *Biochemical Pharmacology*. 28(7):1205-1207, 1979.

Following repeated daily treatment with p-hydroxy-d-amphetamine (pOHdA) in female CD-COBS rats, pOHdA accumulated in the striatum but not in the brainstem. Agents that destroy dopaminergic nerve terminals (6-hydroxydopamine) or release dopamine (reserpine, tetraabenazine, and pimozide) from nerve endings reduced the accumulation of pOHdA in the striatum, but did not affect its level in brainstem or in plasma. Results are compatible with the hypothesis that pOHdA is stored in the striatal dopaminergic system and suggest it may play a role in tolerance to some of the dopaminergic effects of amphetamine. 25 references. (Author abstract modified)

001317 Jork, R.; Grecksch, Gisela; Jirka, Margot; Lossner, B.; Matthies, H. Institute of Pharmacology and Toxicology, Medical Academy, DDR-301 Magdeburg, Germany **Apomorphine and glycoprotein synthesis in rat hippocampus**, *Pharmacology Biochemistry and Behavior*. 12(2):317-318, 1980.

The influence of different doses of apomorphine on incorporation of (3H)-fucose into total proteins of the dorsal hippocampus of rats was investigated. Apomorphine intrahippocampally injected at a dose of 5mcg led to a significant increase in incorporation of (3H)-fucose into total proteins of this brain area. A dose of 40mcg led to a significant decrease in comparison to controls. This provides further evidence for the existence of dopaminergic structures in the hippocampus of rats and their significance for glycoprotein metabolism. 11 references. (Author abstract modified)

001318 Jork, R.; Lossner, B.; Matthies, H. Institute of Pharmacology and Toxicology, Medical Academy, DDR-301 Magdeburg, German Democratic Republic **The influence of cholinergic transmitter substances on the incorporation of (14C)-leucine and (3H)-fucose into the total proteins of hippocampus in vivo and in vitro**, *Pharmacology Biochemistry and Behavior*. 11(2):243-245, 1979.

The influence of cholinergic transmitter substances on the incorporation of 14C-leucine and 3H-fucose into the total proteins of the rat hippocampus was studied in vivo and in vitro. Incorporation of 14C-leucine into the total proteins of hippocampus was inhibited by high concentrations of cholinergic agonists, with nicotinic substances such as 1,1-dimethyl-4-phenyl-piperazine being more effective than muscarinic compounds such as arecoline and pilocarpine. Under these conditions, the incorporation of 3H-fucose was not influenced. 22 references. (Author abstract modified)

001319 Juorio, A. V. Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan S7N 0X0, Canada **Effect of stress and L-DOPA administration on mouse striatal tyramine and homovanillic acid levels**, *Brain Research*. 179(1):186-189, 1979.

Striatal levels of p-tyramine, m-tyramine, and homovanillic acid (HVA) were measured in male Swiss mice subjected to mild stress. Stress induced by aggregation or by cold exposure significantly reduced p-tyramine levels and increased m-tyra-

mine levels. The striatal HVA level was significantly increased in mice subjected to aggregation stress, but not in those subjected to cold stress. Administration of L-DOPA produced a dose dependent, significant reduction in striatal levels of p-tyramine, a significant increase in striatal HVA levels, and no significant change in m-tyramine levels. Chlorpromazine, haloperidol, and d-amphetamine also reduced striatal levels of p-tyramine. Results suggest that p-tyramine may act in the striatum as a modulator or transmitter in controlling the activity of dopaminergic neurons. 23 references.

001320 Kadlubowski, M.; Hughes, R. A. C.; Gregson, N. A. Dept. of Medicine, Guy's Hospital Medical School, London Bridge, London SE1 9RT, England **Experimental allergic neuritis in the Lewis rat: characterization of the activity of peripheral myelin and its major basic protein**, *P2. Brain Research*. 184(2):439-454, 1980.

A P2 preparation is characterized, and the doses of myelin and P2 and adjuvant conditions necessary to produce experimental allergic neuritis (EAN) in the Lewis rat are defined. EAN was produced in the inbred Lewis rat in the absence of experimental allergic encephalomyelitis (EAE) using bovine intradural root myelin. P2 was found to be highly neurotogenic and is probably the sole neurotogenic antigen in this system. The successful demonstration of its neurotogenicity must be due in large part to the use of the inbred Lewis rat and bovine P2, but an explanation could also involve the omission of denaturing organic solvents, the prevention of oxidative denaturation and presumably the fact that any changes which may occur are not sufficient to prevent recognition of the active site by the immune system of the inbred Lewis rat. P2 was neurotogenic down to 5mcg/animal. Its activity was enhanced by but not dependent on the presence of Mycobacterium in the adjuvant. This suggests that release of P2 can possibly break tolerance and produce an autoimmune disease such as the Guillain-Barre syndrome. 43 references. (Author abstract modified)

001321 Kafka, Marian S.; Thoa, Nguyen B. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Alpha-adrenergic receptors in the rat superior cervical ganglion**, *Biochemical Pharmacology*. 28(16):2485-2489, 1979.

The binding of the alpha-adrenergic antagonist (3H)dihydroergocryptine was used to study alpha-adrenergic receptor sites on membranes of male Sprague-Dawley rat superior cervical ganglia. The binding was specific, saturable, reversible, rapid, and stereoselective. Specific binding was displaced by alpha-adrenergic agonists and antagonists, but not by a beta-adrenergic agonist or antagonist. Decentralization of the ganglia (by severing the preganglionic cholinergic nerve supply) resulted in a marked decrease in the number of alpha-adrenergic receptors. Results suggest that about half the alpha-adrenergic receptors are located on preganglionic cholinergic axon terminals and half on ganglionic cell membranes. 18 references. (Author abstract modified)

001322 Kant, G. Jean; Meyerhoff, James L.; Lenox, Robert H. Dept. of Medical Neurosciences, Div. of Neuropsychiatry, Walter Reed Army Institute of Research, Washington, DC 20012 **In vivo effects of apomorphine and 4-(3-butoxy-4-methoxybenzyl)-2-imidazolidinone (R0 20-1724) on cyclic nucleotides in rat brain and pituitary**, *Biochemical Pharmacology*. 29(3):369-373, 1980.

The effect of apomorphine or of 4-(3-butoxy-4-methoxybenzyl)-2-imidazolidinone (R0 20-1724), a potent phosphodiesterase inhibitor on levels of cAMP and cGMP in vivo was examined in the rat pituitary, cerebellum, corpus striatum and nucleus accumbens/olfactory tubercle. Rats were injected with vehicle or

R0 20-1724 (30mg/kg) 30 min prior to injection of saline or apomorphine hydrochloride (1 or 10mg/kg). Animals were killed by microwave irradiation 7 min after the second injection. R0 20-1724 increased levels of cAMP in all four regions, especially in pituitary. R0 20-1724 increased levels of cGMP in cerebellum, but not in pituitary. Apomorphine increased cAMP in the pituitary, and cGMP in all four regions. R0 20-1724 did not produce supra additive effects with apomorphine. The system most responsive to either drug was cAMP in the pituitary, where cAMP increased approximately tenfold after either apomorphine or R0 20-1724. 41 references. (Author abstract)

001323 Karasawa, T.; Furukawa, K.; Ochi, Y.; Shimizu, M. Research Laboratories, Daiinippon Pharmaceutical Co., Ltd., Suita, Osaka 564, Japan. **Monoamine metabolites as indicators of the effect of centrally acting drugs on monoamine release in rat brain.** Archives Internationales de Pharmacodynamie et de Therapie. 231(2):261-273, 1978.

Various central acting drugs were examined for their effects on the levels of brain homovanillic acid (HVA), 3-methoxy-4-hydroxy-phenylethylene glycol sulfate (MOPEG-SO₄), and 5-hydroxy-indoleacetic acid (5-HIAA) in normal rats and on the accumulation of brain 3-methoxy-tyramine (3-MT) and normetanephrine (NM) in pargyline treated rats. Responses to methamphetamine, chlorpromazine, haloperidol, phenoxybenzamine, propranolol, apomorphine, clonidine, cocaine, desipramine, diazepam, and trihexyphenidyl were analyzed. It is suggested that levels of brain HVA, MOPEG-SO₄, and 5-HIAA and the accumulation of 3-MT and NM can be used as an estimate of drug-induced modulation of central monoamine release. 39 references. (Author abstract modified)

001324 Karlen, Bo; Lundgren, Gosta; Lundin, Jan; Holmstedt, Bo. Kabi AB, Research Department, Analytical Chemistry, S-112 87 Stockholm, Sweden. **Effect of physostigmine and atropine on acetylcholine turnover in mouse brain.** Naunyn-Schmiedeberg's Archives of Pharmacology. 308(1):61-65, 1979.

The effect of physostigmine salicylate (0.5mg/kg i.p.), alone or in combination with atropine sulfate (25mg/kg i.p.), on levels of acetylcholine (ACh) and choline (Ch) and on ACh turnover was studied in male NMR mouse whole brain and striatum. Physostigmine increased levels of ACh in whole brain from 24.5 to 28.0nmol/g, but the increase in striatum was not significant. The turnover rate for ACh was decreased in whole brain from 15.4 to 8.4nmol/g/minute and in striatum from 52 to 24.4nmol/g/minute. Physostigmine increased Ch levels in whole brain and striatum, but the increase was more pronounced in whole brain. Physostigmine given before or after atropine did not completely block the ACh lowering effect of atropine. When atropine was given before physostigmine, the turnover rate of ACh in whole brain was increased to 24.2nmol/g/minute. The increase in turnover rate induced by atropine was masked unless a cholinesterase inhibitor was given to protect the newly synthesized ACh. 17 references. (Author abstract modified)

001325 Karobath, M. Salk Institute, P.O. Box 1809, San Diego, CA 92112. **Molecular basis of benzodiazepine actions.** Trends in Neurosciences. 2(7):166-168, 1979.

Research concerned with the minor tranquilizer benzodiazepine and its mechanism of action are reviewed. Electrophysiological and biochemical studies indicate that benzodiazepines exert their pharmacological effects in the central nervous system by interacting with a specific benzodiazepine receptor which is localized on neurons. This receptor is part of a larger complex consisting of several sites including the benzodiazepine receptor, a gamma-aminobutyric acid (GABA) receptor, and the chloride conductance mechanism associated with

the GABA receptor. A number of functional interactions between these sites are described which point to the concept of a more complex and modulated GABA receptor. It is concluded that the benzodiazepines exert their pharmacological effects by altering the functional state of this benzodiazepine/GABA receptor complex. 10 references.

001326 Karobath, Manfred; Lippitsch, Margit. Psychiatrische Universitätsklinik, Lazarettgasse 14, A-1090 Wien, Austria. **THIP and isoguvacine are partial agonists of GABA-stimulated benzodiazepine receptor binding.** European Journal of Pharmacology. 58(4):485-488, 1979.

The effects of 4,5,6,7-tetrahydroisoxazolo(4,5-c)-pyridin-3-ol (THIP) and isoguvacine on the binding of tritiated flunitrazepam to washed membranes prepared from adult rat cerebral cortex were examined. THIP had only minimal stimulatory effects on benzodiazepine (BZ) binding, but inhibited the stimulation induced by small concentrations (2mM) of exogenous GABA. Isoguvacine, stimulated BZ receptor binding and antagonized the stimulation of BZ receptor binding induced by GABA. Results indicate that THIP and isoguvacine act as partial agonists of GABA stimulated BZ receptor binding. 10 references. (Author abstract modified)

001327 Karobath, Manfred; Rogers, Joseph; Bloom, Floyd E. Bloom: Alcohol Research Center, Salk Institute, P.O. Box 85800, San Diego, CA 92138. **Benzodiazepine receptors remain unchanged after chronic ethanol administration.** Neuropharmacology. 19(1):125-128, 1980.

Brain homogenates of Sprague-Dawley rats subjected to ethanol inhalation for 19 days (mean blood ethanol, 258mg/100ml) showed 3H-flunitrazepam binding virtually identical to that of ethanol naive controls. GABA stimulation of 3H-flunitrazepam binding was also nearly identical in the ethanol and control groups. Results suggest that the clinical interaction between benzodiazepines and ethanol is not mediated through primary binding sites for the benzodiazepines. 10 references. (Author abstract modified)

001328 Karoum, Farouk; Speciale, Samuel G., Jr.; Neff, Norton H. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeth's Hospital, Washington, DC 20032. **3,4-Dihydroxyphenylacetic acid content of sympathetic ganglia as a possible biochemical indicator of small intensely fluorescent cell participation in ganglionic transmission.** Biochemical Pharmacology. 29(1):118-119, 1980.

The 3,4-dihydroxyphenylacetic acid content of sympathetic ganglia was investigated as a possible biochemical indicator of small intensely fluorescent cell participation in ganglionic transmission. It is demonstrated that drugs that interact with cholinergic, adrenergic, and dopaminergic receptors alter the metabolism of dopamine (DA) in the celiac ganglion of the rat. The finding that phenylephrine reduces DA metabolism suggests a model of the release of DA in the small intensely fluorescent (SIF) cells of sympathetic neurons onto principal neurons. It is suggested that DA acting via a negative neuronal feedback loop and norepinephrine released from the principal neurons might alter the release and metabolism of DA by the SIF cells. Moreover, results suggest that drugs that alter dihydroxyphenylacetic acid content in ganglia might be identified for further study on ganglionic transmission. 6 references.

001329 Kastin, Abba J.; Olson, Richard D.; Schally, Andrew V.; Coy, David H. V.A. Medical Center, Tulane University School of Medicine, New Orleans, LA 70146. **CNS effects of peripherally administered brain peptides.** Life Sciences. 25(5):401-414, 1979.

The family of brain peptides including enkephalins and endorphins, which are characterized by their multiple and independent effects, are considered in a review of the literature and of recent research. The concept that the multiple actions of peptides can be independent of each other is supported by evidence that even though peripheral administration of the brain opiates is essentially ineffective in producing analgesia, other actions of these peptides, such as changes in behavior, can be observed after administration by this route. The mechanisms by which the central effects of the peptides are exerted after systemic injection remain to be clarified, but analysis of their actions represents a new approach to understanding the performance of the brain. Studies suggest a possible role of the brain peptides in the diagnosis and treatment of some mental and neurological disorders as well as in optimizing normal CNS functions. 167 references. (Author abstract modified)

001330 Kayaalp, S. Qguz; Neff, Norton H. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Cholinergic muscarinic receptors of bovine adrenal medulla**. *Neuropharmacology*. 18(11):909-911, 1979.

Muscarinic receptor binding sites were identified on bovine adrenal medulla membranes, using (3H)-quinuclidinyl benzylate. A Scatchard analysis revealed a dissociation constant of 0.07nM and a maximum binding capacity of 3fmol/mg protein. Muscarinic receptors of the medulla may be partially responsible for the release of catecholamines and the modulation of the cyclic nucleotide content of chromaffin cells. 10 references. (Author abstract)

001331 Kerwin, Robert; Pycock, Christopher. Dept. of Pharmacology, Medical School, University of Bristol, Bristol, BS8 1TD, England **Effects of omega-amino acids on tritiated dopamine release from rat striatum: evidence for a possible glycinergic mechanism**. *Biochemical Pharmacology*. 28(14):2193-2197, 1979.

Glycine (doses above 200mM) and GABA (doses above 50mM) released tritiated dopamine from prelabelled slices of female Porton rat striatum, but had no effect on the release of radiolabeled 5-hydroxytryptamine or GABA. The GABA antagonist picrotoxin (50mM) markedly reduced the ability of GABA to release (3H)dopamine, but had no effect on the glycine response. Strychnine (0.5mM), which acts as a specific glycine receptor antagonist at low concentrations, abolished the effects of both GABA and glycine on (3H)dopamine release. Taurine and beta-alanine, both at 500mM, had no effect on (3H)dopamine release from rat striatal slices. Additional experiments demonstrated the calcium dependent release of radioactivity from neonatal rat spinal cord and striatal slices after prelabeling with (3H)glycine. The possibilities that glycine may act as a transmitter within the striatum and that GABA may exert some of its pharmacological effects through the glycine receptor are discussed. 21 references. (Author abstract modified)

001332 Key, B. J.; Boakes, R. J.; Candy, J. M. MRC Neuropharmacology Unit, Medical School, Birmingham, B15, England **Responses of cat dorsal raphe neurons to iontophoretically applied noradrenaline**. *Neuropharmacology*. 19(1):139-142, 1980.

The effects of iontophoretically applied noradrenaline (NA) on neurons of the dorsal raphe nucleus (DRN) were examined in cats, using iontophoretic injection of dye to locate and identify the test neurons. A high proportion of spontaneously firing neurons within the DRN responded to NA, but the nucleus appeared to contain more than one pharmacologically distinct group of neurons. Most of the responsive neurons were inhibited by NA, but those in the ventral portion of the DRN showed excitatory responses. 11 references.

001333 Khanna, Jatinder M.; Le, Anh D.; Kalant, Harold; Leblanc, A. Eugene. Dept. of Pharmacology, University of Toronto, Toronto, Ontario, Canada M5S 1A8 **Cross-tolerance between ethanol and morphine with respect to their hypothermic effects**. *European Journal of Pharmacology*. 59(1/2):145-149, 1979.

Daily administration of ethanol (10 to 12g/kg) in a liquid diet to male Wistar rats resulted in tolerance to the hypothermic effects of ethanol. The rats also developed cross-tolerance to the hypothermic effects of 15 or 30mg/kg morphine, but not to the hyperthermic effect of 5mg/kg morphine. Administration of 30mg/kg morphine for 3 days resulted in tolerance to morphine hypothermia and cross-tolerance to the ethanol-induced hypothermia. These findings are consistent with the hypothesis that tolerance and cross-tolerance among drugs develop to drug effects rather than to the drugs per se. 10 references. (Author abstract modified)

001334 Kiely, M. E. Department of Psychiatry, Montreal General Hospital, 1650 Cedar Avenue, Montreal, Quebec H3G 1A4, Canada **Effect of hypophysectomy adrenalectomy and glucocorticoids on tryptophan accumulation by rat cerebral cortex slices**. *Research Communications in Psychology, Psychiatry and Behavior*. 5(1):49-60, 1980.

The effect of adrenalectomy, hypophysectomy, hydrocortisone, and dexamethasone on tryptophan transport into rat cerebral cortex slices was investigated. The accumulation of L-tryptophan was not significantly different in tissue slices from animals which had undergone either adrenalectomy or hypophysectomy as compared with tissue slices from sham operated rats. The presence of dexamethasone or hydrocortisone in the incubation medium did not change the net uptake of tryptophan by cerebral cortex slices from normal animals. It was concluded that glucocorticoids do not play a role in tryptophan transport across the brain cell membrane of cerebral cortex tissue. 23 references. (Author abstract)

001335 Kiyono, S.; Seo, M.; Shibagaki, M. Dept. of Physiology, Institute for Developmental Research, Aichi Prefectural Colony for the Handicapped, Kasugai, Aichi 480-03, Japan **Sleep-waking cycle in microencephalic rats induced by prenatal methylazoxymethanol application**. *Electroencephalography and Clinical Neurophysiology*. 48(1):73-79, 1980.

The sleep/wakefulness cycle of adult male Sprague-Dawley rats that had been made microencephalic by administration of methylazoxymethanol acetate (MAM) on day 15 of gestation was examined. Rats treated prenatally with 20mg/kg MAM did not differ from control rats. But those treated with 25mg/kg MAM showed a significant decrease in paradoxical sleep (PS) and in the ratio of PS to total sleep time. The MAM treated, microencephalic rats showed a significant increase in spindle bursts during PS, suggesting PS is not as deep in these animals as in normal rats. 27 references.

001336 Klotz, U. Dr. Margarete Fischer-Bosch-Institut für Klinische Pharmakologie, Auerbachstrasse 112, D-7000 Stuttgart 50, Germany **Effect of age on levels of diazepam in plasma and brain of rats**. *Naunyn-Schmiedeberg's Archives of Pharmacology*. 307(2):167-169, 1979.

The concentrations of diazepam in plasma, cerebellum, and brain of middle aged (6 months) and old (18 months) male Wistar rats following i.v. injection of 5mg/kg diazepam were determined. Diazepam was eliminated more slowly in the old rats (elimination half-life, 3.1 hours) than in middle aged rats (half-life, 1.4 hours), due to an increase in the apparent volume of distribution. Concentrations of diazepam in brain and cerebellum were in the same range (0.5 to 1.1ng/mg) in both age groups. It is concluded that distribution of diazepam is age de-

pendent and possibly related to altered body composition in older rats. 15 references. (Author abstract modified)

001337 Knapp, Suzanne; Mandell, A. J. Dept. of Psychiatry, University of California, San Diego, La Jolla, CA 92093 Lithium and chlorimipramine differentially alter bilateral asymmetry in mesostriatal serotonin metabolites and kinetic conformations of midbrain tryptophan hydroxylase with respect to tetrahydrobiopterin cofactor. *Neuropharmacology*. 19(1):1-7, 1980.

Lithium decreased and chlorimipramine (CMI) differentially altered hemispheric asymmetries in striatal and hippocampal concentrations of tryptophan, serotonin, and 5-hydroxyindoleacetic acid (5-HIAA) in the Sprague-Dawley rat brain. The kinetic functions of tryptophan hydroxylase from the two halves of the midbrain, demonstrated by pteridine cofactor (BH4) kinetic functions, also changed differentially in response to the two drugs. Bilateral asymmetries in 5-HIAA and kinetic functions with regard to BH4 after CMI administration suggest that CMI may alter the relative serotonergic activity of the two hemispheres. In contrast, lithium evoked similar tryptophan hydroxylase functions with regard to BH4 from both hemispheres and reduced asymmetries in metabolites, which is more suggestive of a bilaterally simultaneous biochemical field mechanism. 31 references. (Author abstract modified)

001338 Kogure, K.; Schwartzman, R. J. Cerebral Vascular Disease Research Center, Dept. of Neurology, University of Miami School of Medicine, Miami, FL 32600 Seizure propagation and ATP depletion in the rat stroke model. *Epilepsia*. 21(1):63-72, 1980.

Cerebral infarction was produced in rats by internal carotid injection of 35mc plastic microspheres, and regional concentration of endogenous brain ATP was studied by the histochemical bioluminescent method. Electroencephalograms were recorded through the scalp and from the thalamus. Following embolization, a specific pattern of seizure propagation was noted. Spike activity appeared first in the contralateral hemisphere, then the contralateral thalamus, infarcted thalamus, and finally in the cortex. The results of these experiments suggest that seizure activity following an evolving focal ischemic injury in the brain appears in the face of lowered ATP content. 24 references. (Author abstract modified)

001339 Kohler, Christer; Fuxe, Kjell; Ogren, Sven-Ove; Agnati, Luigi. Research Laboratories, Astra Lakemedel AB, Södertälje, Karolinska Institute, Stockholm, Sweden Evidence for in vivo binding of apomorphine and bromocriptine to receptor sites not labelled by 3H-spiroperone. *European Journal of Pharmacology*. 58(3):339-340, 1979.

The in vivo displacement of 3H-spiroperone binding in male Sprague-Dawley rat brain by the dopamine (DA) agonists apomorphine and bromocriptine was examined. After saturation of central 3H-spiroperone binding in vivo, the two DA agonists failed to reduce antagonist binding in several brain regions, including the striatum. At the same dose levels, both apomorphine and bromocriptine elicited behavioral stereotypies previously attributed to the stimulation of striatal and limbic DA receptors. These findings indicate that DA receptor agonists can produce their behavioral effects without displacing the DA antagonist 3H-spiroperone from its striatal binding sites, which suggests that the agonist and antagonist binding sites of the DA receptor are separate entities. 5 references.

001340 Kondo, Yasuro; Iwatsubo, Katsuya. Iwatsubo: Dept. of Pharmacology, Osaka University Dental School, Kita-ku, Osaka 530, Japan Diminished responses of nigral dopaminergic neurons to haloperidol and morphine following lesions in the striatum. *Brain Research*. 181(1):237-240, 1980.

The effects of haloperidol and morphine on the firing of dopaminergic (DA) neurons in the substantia nigra zona compacta were determined in male rats given kainic acid lesions of the striatum. Haloperidol (0.05mg/kg i.v.) enhanced firing rates in about 95% of DA neurons tested in control animals, but increased firing of only 20% of DA neurons tested in the lesioned animals. Morphine (5mg/kg i.v.) increased DA cell firing of more than 90% of cells tested in control rats, but in only 37.5% of the cells in lesioned animals. The mean firing rates of the tested cells were not altered by either drug in the lesioned animals. 24 references.

001341 Korczyn, Amos D.; Keren, Ora. Dept. of Physiology and pharmacology, Sackler School of Medicine, Tel Aviv University, Ramat Aviv, Israel. The effect of dopamine on the pupillary diameter in mice. *Life Sciences*. 26(10):757-763, 1980.

The effect of dopamine on the pupillary diameter of the mouse was investigated. Dopamine and adrenaline injected into mice produce dose related mydriasis. The effects of both dopamine and adrenaline are antagonized similarly by the alpha-adrenergic blocking agents phentolamine and thymoxamine as well as by haloperidol, but are not prevented by pretreatment with reserpine. These results suggest that in mice, dopamine produces mydriasis by direct stimulation of alpha-adrenergic receptors in the dilator iridis. 14 references. (Author abstract modified)

001342 Korf, Jakob; Sebens, Jantien B.; Postema, Folkert. Dept. of Biological Psychiatry, Oostersingel 59, 9713 EZ Groningen, The Netherlands Cyclic AMP in the rat cerebral cortex after stimulation of the locus coeruleus: decrease by antidepressant drugs. *European Journal of Pharmacology*. 59(1/2):23-30, 1979.

The effect of repeated treatment with antidepressant drugs on the elevation of cyclic AMP levels in the male Wistar rat cortex following electrical stimulation of the locus coeruleus was examined. Desmethylinipramine (5mg/kg/day for 2 weeks) was the most potent drug in inhibiting the cyclic AMP response to stimulation. At a daily dose of 10mg/kg for 2 weeks, imipramine and nomifensine produced slight decreases in the cyclic AMP responses, while ipindol and clomipramine were ineffective. Ipindol, clomipramine, and mianserin were without effect after daily 10mg/kg doses for 6 weeks, but the cyclic AMP response was suppressed by higher doses (20mg/kg/day for 2 weeks) of clomipramine or mianserin. Results indicate that tricyclic and tetracyclic antidepressant drugs are able to decrease cerebral noradrenergic transmission of locus coeruleus neurons, but it is not clear that this modification is related to the therapeutic action of the drugs. 48 references. (Author abstract modified)

001343 Koroleva, V. I.; Bures, J. Institute of Higher Nervous Activity and Neurophysiology, Academy of Sciences of USSR, Moscow, USSR Blockade of cortical spreading depression in electrically and chemically stimulated areas of cerebral cortex in rats. *Electroencephalography and Clinical Neurophysiology*. 48(1):1-15, 1980.

The penetration of cortical spreading depression (SD) into epileptic foci established in male hooded rat cortex by penicillin or metrazol and into electrically stimulated cortical regions was examined. SD suppressed the activity of penicillin foci with low rates of interictal discharge (0.3Hz) but did not invade more active foci (1Hz) or foci triggered by electrical stimulation (1 to 3Hz). Metrazol foci did not block SD propagation when applied at 6 to 10Hz. Repetitive direct cortical responses elicited by 0.05 to 0.1msec pulses blocked SD propagation when applied at 6 to 10Hz. for 5 to 20 minutes. SD propagation appeared to be prevented by enhanced potassium ion reabsorption which rapidly

removed potassium ions penetrating the stimulated areas from the SD front. 44 references.

001344 Koss, M. C.; Bernthal, P. L. Dept. of Pharmacology, University of Oklahoma, Health Sciences Center, P. O. Box 26901, Oklahoma City, OK 73190 **Potential of two sympathetic reflexes by yohimbine hydrochloride.** *Neuropharmacology*. 18(3):295-300, 1979.

Yohimbine hydrochloride (0.5mg/kg i.v.) produced a marked increase in electrodermal and nictitating membrane reflexes in intact anesthetized and decerebrate unanesthetized cats, but not in spinal preparations. The potentiation of these two sympathetic reflexes was observed in baroreceptor denervated cats, indicating the effect was not due to lowering of blood pressure. Yohimbine also appeared to increase central tonic activity with regard to basal skin potential, nictitating membrane basal tone, and heart rate levels. 23 references. (Author abstract modified)

001345 Kostrzewa, Richard M.; Hardin, Judy C.; Snell, Robert L.; Kastin, Abba J.; Coy, David H.; Bymaster, Frank. Dept. of Pharmacology, East Tennessee State University College of Medicine, Johnson City, TN 37601 **MIF-I and postsynaptic receptor sites for dopamine.** *Brain Research Bulletin*. 4(5):657-662, 1979.

The action of l-prolyl-l-leucyl-glycine amide (MIF-I) on post-synaptic components of male Sprague-Dawley rat striatal dopaminergic nerves was studied in an attempt to elucidate the tripeptide's antiparkinsonian effect. Tyrosine hydroxylase, dopa decarboxylase, choline acetyltransferase, and glutamic acid decarboxylase activities in the striatum were not altered by a series of five injections of MIF-I (1mg/kg i.p. each, at 24 hour intervals). No changes in adenylate cyclase, dopamine stimulated adenylate cyclase, or guanylate cyclase were observed in vitro in response to various concentrations of MIF-I (0.1 to 1000mM). MIF-I also failed to alter the rate of uptake of 3-H-dopamine by rat striatal synaptosomes or the binding of 3H-dopamine and 3H-spiperone to beef caudate membranes. These findings indicate that MIF-I does not act directly on striatal dopamine post-synaptic receptors and suggest that the substance produces its antiparkinsonian effect indirectly or by an action on a nondopaminergic or nonstriatal component of brain. 33 references. (Author abstract modified)

001346 Kozaki, Shunji. College of Agriculture, University of Osaka Prefecture, Sakai-shi, Osaka 591, Japan **Interaction of botulinum type A, B and E derivative toxins with synaptosomes of rat brain.** *Nahyn-Schmiedeberg's Archives of Pharmacology*. 308(1):67-70, 1979.

Clostridium botulinum 125I-labeled derivative toxin immediately bound to rat brain synaptosomes. Of the two fragments of type-B derivative toxin, the large molecular weight fragment inhibited the binding of labeled type-B derivative toxin to synaptosomes in the same manner as unlabeled type-B toxin did. The inhibition by the small molecular weight fragment was less than that by the large molecular weight fragment. Results suggest that type-B binds to synaptosomes mainly with some part of the large molecular weight fragment. The binding of labeled type-A and type-E derivative toxins was inhibited by unlabeled type-A or type-E derivative toxins, but not by type-B derivative toxin. It is concluded that synaptosomes of rat brain possess relatively specific binding sites for botulinum toxin types. 22 references. (Author abstract)

001347 Kozhechkin, S. N. Institute of Pharmacology, Academy of Medical Sciences of the USSR, Moscow, USSR **Gamma-hydroxybutyrate potentiates the action of dopamine.** *Neuropharmacology*. 18(11):917-920, 1979.

The effects of microiontophoretically applied sodium hydroxybutyrate (GHB) and dopamine (DA) on the spontaneous, extracellularly recorded electrical activity of frontal cortical neurons were studied in rabbits. Both agents produced predominantly inhibitory effects on neuronal activity. The inhibitor effect of DA was potentiated by subthreshold doses of GHB. GHB prevented the escape of neurons from the inhibitory effect of DA and increased the duration of recovery of cellular activity after the application of DA was stopped. It is suggested that GHB prevents the process of DA inactivation. 4 references. (Author abstract modified)

001348 Krause, Diana N.; Wong, Esther; Degener, Phyllis; Roberts, Eugene. Division of Neurosciences, City of Hope National Medical Center, Duarte, CA 91010 **GABA receptors in bovine cerebral blood vessels: binding studies with (3H)muscimol.** *Brain Research*. 185(1):51-57, 1980.

The specific binding of tritiated muscimol to sites in a crude membrane fraction prepared from bovine cerebral blood vessels was saturable and of high affinity. It was selectively inhibited by GABA, specific GABA agonists, and bicuculline, with potencies similar to those reported for GABA receptors in mammalian brain. The pharmacology of the (3H)muscimol binding site correlated well with the vasodilatory response to GABA and related drugs. No significant specific (3H)muscimol binding was detected in aorta and mesenteric arteries. The characteristics of the cerebrovascular muscimol binding site suggest a physiologically relevant GABA receptor is associated with the cerebral blood vessels and may be involved in cerebral vascular function. 22 references. (Author abstract modified)

001349 Kriegstein, Josef; Rieger, Hubert; Schutz, Hartmut. Institut für Pharmakologie und Toxikologie, Philipps-Universität Marburg, Ketzertbach 63, D-3550 Marburg, Germany **Comparative study on the activity of chlorpromazine and 7-hydroxychlorpromazine in the isolated perfused rat brain.** *Biochemical Pharmacology*. 29(1):63-67, 1980.

The actions of chlorpromazine (CPZ), 7-hydroxychlorpromazine (7-OH-CPZ), 8-hydroxychlorpromazine, 3,7-dihydroxychlorpromazine, and chlorpromazine sulfoxide on isolated perfused rat brain were investigated. Isolated rat brains were perfused for 30 minutes with a perfusion medium containing approximately 30% bovine red cells, 2 g bovine serum albumin, 14 mM glucose, and one of the phenothiazines in a concentration of 5 to 100 mcm. The main dopamine metabolite, homovanillic acid (HVA), was measured fluorimetrically in the striatum of the isolated brain. The EEG was recorded with two symmetrical bipolar leads from the parietal regions at various times and was stored on a magnetic tape. The recordings were evaluated visually and quantitatively by automatic analysis. CPZ and 7-OH-CPZ changed the EEG and increased the striatal HVA level significantly but CPZ seemed to be more active. The other phenothiazines studied did not produce clear effects. The increase of the HVA level in the striatum was correlated with the increase of the EEG amplitude and of the percentages of theta and delta waves as well as with the decrease in the percentage of beta waves. 23 references. (Author abstract modified)

001350 Krishnan, Hema; Baquer, Najma Z.; Singh, Rameshwar. Neurochemistry Unit, School of Life Sciences, Jawaharlal Nehru University, New Delhi-110 067, India **Effect of ketamine hydrochloride on the activity of Na-KATPase in the synaptosomal fraction of rat brain.** *Research Communications in Chemical Pathology and Pharmacology*. 27(3):615-618, 1980.

Ketamine significantly reduced the activity of sodium and potassium dependent adenosine triphosphatase (ATPase) in synap-

tosomes of female Wistar rat brain, both in vivo and vitro. The in vitro inhibition was noncompetitive. The role of ATPase inhibition in neurotransmitter events at synapses is discussed. 13 references. (Author abstract modified)

001351 Krnjevic, K.; Reinhardt, W. Dept. of Anaesthesia Research, McGill University, Montreal, Quebec H3G 1Y6, Canada **Choline excites cortical neurons.** Science. 206(4424):1321-1323, 1979.

The finding that in an investigation of cortical cholinergic neurons, choline was found to be a weak excitant of ACh-sensitive cells was reinvestigated. In cats under halothane or methoxyflurane, iontophoretic applications of choline are only eight times weaker than applications of acetylcholine in evoking firing of neurons in the sensorimotor region of the cerebral cortex. The action of choline is suppressed by atropine but not by two agents that block choline uptake and is not potentiated by an anticholinesterase. Choline therefore appears to excite cortical neurons by a direct action, which may be a significant component of its beneficial therapeutic effects. 19 references. (Author abstract modified)

001352 Krooth, Robert S.; Hsiao, Wen-Luan; Lam, George F. M. Dept. of Human Genetics and Development, College of Physicians and Surgeons, Columbia University, New York, NY 10032 **Effect of 6-azauracil, and of certain structurally similar compounds, on three pyridoxal-phosphate requiring enzymes involved in neurotransmitter metabolism.** Biochemical Pharmacology. 28(7):1071-1076, 1979.

The effects of 6-azauracil and structurally related compounds on the pyridoxal phosphate requiring enzymes glutamic acid decarboxylase (GAD), GABA-transaminase (GABA-T), and DOPA decarboxylase were examined. GABA-T activity in Wistar rat, C57/Bl6J mouse, and human brain extracts was competitively inhibited by 6-azauracil, which has a hypnotic effect in all three species. GABA-T was noncompetitively inhibited by a number of other compounds that alter arousal and include within their structures a pyrimidine or pyrimidine-like ring. GAD was only weakly and (noncompetitively) inhibited by 6-azauracil and the other compounds. None of the substances tested significantly inhibited DOPA decarboxylase activity except under conditions where the enzyme was highly unstable. 38 references. (Author abstract modified)

001353 Kuschinsky, W.; Suda, S.; Sokoloff, L. Laboratory of Cerebral Metabolism, Bldg. 36, 9000 Rockville Pike, NIMH, Bethesda, MD **Effects of metabolic acidosis on local cerebral glucose utilization in rats.** (Unpublished paper). Bethesda, MD, NIMH, 1979. 1 p.

Metabolic acidosis was induced in rats by including 0.35M NH₄Cl in the drinking water for 5 days, and the rate of local cerebral glucose utilization (LCGU) was measured by means of the 2-deoxy-D(14C)glucose method in both experimental and control animals in the conscious state. The acidotic rats were alert and noncomatose. The rates of LCGU were determined in 37 brain regions including six areas of the cerebral cortex and various structures in the midbrain, brainstem, and the cerebellum. In all structures tested, a reduction in LCGU was obtained during metabolic acidosis as compared to 69 micromole/100g/min in the control group. This difference was statistically significant. The experiments show a significant reduction of CGU throughout the brain during prolonged metabolic acidosis. (Author abstract modified)

001354 Lai, Allen A.; Levy, Rene H. Levy: School of Medicine, University of Washington, Seattle, WA 98195 **Pharmacokinetic description of drug interactions by enzyme induction: car-**

bamazepine-clonazepam in monkeys. Journal of Pharmaceutical Sciences. 68(4):416-421, 1979.

The applicability of a pharmacokinetic model for drug interactions by enzyme induction was tested in rhesus monkeys using a design in which the inducer (carbamazepine) and the induced agent (clonazepam) were both infused chronically. The addition of carbamazepine caused the preinduction clonazepam steady-state level to decrease exponentially to a lower steady-state after lag times of 14 to 60.5 hours, and the removal of carbamazepine caused induced clonazepam steady-state levels to climb exponentially to a higher steady-state after lag times of 34 to 81 hours. The extent of induction ranged from 23 to 54%. Induced clonazepam half-lives were significantly shorter than control values. Urinary excretion of D-glucuronic acid was two to three times higher during carbamazepine administration. 33 references. (Author abstract modified)

001355 Lai, James C. K.; Guest, Julian F.; Leung, Thomas K. C.; Lim, Louis; Davison, Alan N. Miriam Marks Dept. of Neurochemistry, Institute of Neurology, National Hospital, Queen Square, London WC1N 3BG, England **The effects of cadmium, manganese and aluminum on sodium-potassium-activated and magnesium-activated adenosine triphosphatase activity and choline uptake in rat brain synaptosomes.** Biochemical Pharmacology. 29(2):141-146, 1980.

The effects of cadmium (Ca), manganese (Mn), and aluminium (Al) ions on rat brain synaptosomal sodium/potassium activated and magnesium activated adenosine triphosphatase (Na/K ATPase and Mg ATPase) activity and choline uptake were studied. All three types of metal ions inhibited Na/K ATPase activity more markedly than Mg ATPase activity. The rank order of inhibition of Na/K ATPase was Cd, Mn, and Al. The rank order of inhibition of Mg ATPase was Cd, Mn, and Al. Al was most potent in inhibiting synaptosomal choline uptake. Cd was a more effective inhibitor of choline uptake than Mn. The presence of Ca did not alter choline uptake, nor did it antagonize the inhibitory actions of the three metals. The observation that Cd and Al inhibited synaptosomal choline uptake, but did not show parallel inhibitory effects on Na/K ATPase activity directly contradicts the ionic gradient hypothesis. These results are discussed in relation to the in vivo neurotoxicity of Cd, Mn, and Al. 21 references. (Author abstract modified)

001356 Lancaster, Francine; Fenimore, David; Samorajski, T. Texas Woman's University, Houston, TX 77030 **Effects of dihydroergotoxine (Hydergine) on peripheral blood alcohol levels.** Life Sciences. 26(4):285-290, 1980.

The effects of dihydroergotoxine (DHET) on peripheral ethanol levels were examined in adult female mice administered 2g/kg ethanol alone or in combination with DHET (2, 4, or 8mg/kg). Blood was drawn after 1 day ethanol administration (acute study) and again after 21 days (chronic study). An additional group of mice received a single dose of ethanol (2g/kg) and DHET (2mg/kg) 15 min apart, with either ethanol or DHET administered first. Blood samples were collected at 5, 15, 30, 60, 120, or 180 min after treatment. Results indicated that: 1) combining ethanol with DHET significantly reduced blood ethanol levels compared to administration of ethanol alone; 2) chronic conditions produced higher blood ethanol levels; and 3) administration of ethanol 15 min before DHET produced a 27% lowering of peripheral blood ethanol levels compared to the reverse order of administration. Data suggest that DHET may be useful in alleviating some of the symptoms associated with alcohol intoxication. 13 references. (Author abstract modified)

001357 Langer, J.; Seeber, U.; Kuschinsky, K.; Sontag, K.-H. Kuschinsky: Max-Planck-Institut für Exp. Medizin, Abt. Biochemische Pharmakologie, Hermann-Rein Str. 3, D-3400, Göttingen, Germany **Effect of haloperidol on reflex activation of rat alpha-motoneurons: a possible explanation for akinesia and catalepsy?** Naunyn-Schmiedeberg's Archives of Pharmacology. 308(2):149-154, 1979.

The effects of haloperidol on rat flexor and extensor alpha-motoneurons were studied in ventral roots of anesthetized, laminectomized rats. Haloperidol in doses of .075, .15, and .30 mg/kg ip inhibited reflex activation of flexor alpha-motoneurons; higher doses appeared more effective than lower ones. Apomorphine (2mg/kg sc) partially antagonized the inhibitory action of haloperidol with some latency. Higher doses of haloperidol (.15 to .60mg/kg ip) also inhibited the reflex of extensor motoneurons; this effect was, at least for a short time, antagonized by apomorphine. Results suggest that akinesia and catalepsy induced in rats by haloperidol might be, at least in part, due to a decrease in sensitivity of alpha-motoneurons to proprioceptive stimuli. 11 references. (Author abstract modified)

001358 Lasala, John M.; Cicero, Theodore J.; Coscia, Carmine J. E. A. Doisy Dept. of Biochemistry, St. Louis University School of Medicine, St. Louis, MO 63104 **Opiate-like effects of norlaudanolinecarboxylic acids on the hypothalamic-pituitary-gonadal axis.** Biochemical Pharmacology. 29(1):57-61, 1980.

The opiate-like effects of norlaudanolinecarboxylic acid (NLCA), a condensation product of dopamine and 3,4-dihydroxyphenylpyruvic acid, on the hypothalamic/pituitary/gonadal axis were investigated both in vitro and in vivo in rats. The ability of NLCA to displace radiolabeled naloxone was measured in the presence and absence of NaCl. A large sodium shift suggest that NLCA is a relatively pure opiate agonist. Two analogs of NLCA, 3'-O-methyl NLCA (MNLCA) and 3',4'-deoxy-NLCA (DNLCA), that have been shown to accumulate during L-dopa chemotherapy of parkinsonism and phenylketonuria, respectively, also behaved as opiate agonists, but the concentrations required were higher than for NLCA. In addition, NLCA, like many opiates, decreased serum luteinizing hormone (LH) levels by approximately 50% in both castrated and normal rats, 1 to 2 hours after its subcutaneous administration. Similarly, in normal males, serum testosterone levels were markedly depressed (60%) after treatment with NLCA. The NLCA-induced depression in serum LH was found to be naloxone reversible. 31 references. (Author abstract modified)

001359 Laverty, R.; Roth, R. H. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Clonidine reverses the increased norepinephrine turnover during morphine withdrawal in rats.** Brain Research. 182(2):482-485, 1980.

The effects of clonidine on norepinephrine (NE) turnover in male Sprague-Dawley rat brain were determined during morphine dependence and naloxone precipitated withdrawal. Clonidine produced a dose dependent reduction in NE turnover in morphine dependent animals, with a significant reduction observed after subcutaneous doses of clonidines small as 10mcg/kg. Clonidine (0.2mg/kg) also suppressed the increase in NE turnover induced by naloxone. The effects of clonidine on NE turnover were evident in all brain regions examined and were significant in all regions except the hypothalamus. Results suggest that clonidine may be of use in relieving symptoms of opiate withdrawal. 8 references.

001360 Le Bars, D.; Rivot, J. P.; Guilbaud, G.; Menetrey, D.; Besson, J. M. Unité de Recherches de Neurophysiologie Pharmacologique de l'INSERM (U 161), 2, rue d'Alesia, F-75014 Paris, France **The depressive effect of morphine on the C fibre re-**

sponse of dorsal horn neurones in the spinal rat pretreated or not by pCPA. Brain Research. 176(2):337-353, 1979.

The effects of morphine on the transmission of nociceptive messages at the spinal level were investigated in spinal male Sprague-Dawley rats. The responses of dorsal horn cells to activation of C-fibers were depressed in a dose dependent fashion in all cases, and this effect was reversed by naloxone. Responses to A/delta-fibers were also depressed dose dependently, but those to A/alpha-fibers were not affected. In rats pretreated with the serotonin synthesis inhibitor parachlorophenylalanine, two thirds of the cells showed a dose response curve similar to that seen in untreated animals, but the remaining third was not affected by morphine or naloxone. The lowering of spinal cord serotonin content was associated with a 34% decrease in the size of the excitatory receptive field and a 36% decrease of activities related to C-fiber input of the dorsal horn cells. Results suggest that two mechanisms are involved in the depressive effects of morphine at the spinal level, one of which involves serotonergic terminals. 101 references. (Author abstract modified)

001361 Le Bars, Daniel; Dickenson, Anthony H.; Besson, Jean Marie. Unité de Recherche de Neurophysiologie Pharmacologique de l'INSERM (U. 161), 2, rue d'Alesia, F-75014 Paris, France **Microinjection of morphine within nucleus raphe magnus and dorsal horn neurone activities related to nociception in the rat.** Brain Research. 189(2):467-481, 1980.

The hypothesis of an increase by morphine of descending inhibitory controls acting upon the transmission of painful messages at the spinal level was investigated in intact anesthetized rats via microinjection of morphine within nucleus raphe magnus (NRM) and observation of analgesic efficacy in the vocalization threshold after electric tail shock. A mean threshold increase of 57% was observed. A few days later, the effects of similar microinjections upon dorsal horn cell activities were studied in acute experiments in the same animals. The response of dorsal horn convergent units induced by the activation of large myelinated (Alpha) afferent fibers were unaffected by the microinjection of morphine within the NRM. In the case of the responses of convergent units induced by the activation of unmyelinated (C) afferent fibers, two different results were obtained after microinjection of morphine within the NRM: 8/14 units were not affected and 6/14 were clearly excited. A transient reversal of the excitatory effects was observed after the systemic administration of the opiate antagonist naloxone. Responses of marginal layer cells (lamina I) were unaffected by the microinjection of morphine within the NRM. These unexpected results are discussed in view of the fact that they conflict with current concepts regarding morphine analgesia. 64 references. (Author abstract modified)

001362 Le Fur, G.; Phan, T.; Uzan, A. Pharmindustrie. Groupe PHARMUKA, 35, quai du Moulin de Cage, F-92231, Gennevilliers, France **Identification of stereospecific (3H)spiroperidol binding sites in mammalian lymphocytes.** Life Sciences. 26(14):1139-1148, 1980.

Dopaminergic receptors in mammalian lymphocytes were identified using (3H)spiroperidol as a specific ligand. The specific binding is saturable with two components ($KD1 = 1.9$ nM, $KD2 = 36.2$ nM). Determination of the KD by kinetic studies measuring rate constants for association and dissociation provided KD values similar to those obtained in equilibrium experiments. The specific binding is proportional to cell concentration and temperature dependent with a maximum at 37°C. The relative potencies of different antidopaminergic agents in competing for (3H) spiroperidol binding sites parallel their activity in the striatum. It is concluded that the lymphocyte dopaminergic re-

ceptors could be implicated in lymphocytes mediated immune response. 25 references. (Author abstract modified)

001363 Le Fur, Gerard; Guilloux, Francoise; Uzan, Andre. Pharmindustrie, PHARMUKA, 35 quai du Moulin de Cage, F-92231 Gennevilliers, France *In vivo* blockade of dopaminergic receptors from different rat brain regions by classical and atypical neuroleptics. *Biochemical Pharmacology*. 29(3):267-270, 1980.

The effect of haloperidol, chlorpromazine, clozapine, benzamides (sulpiride and isosulpiride) and 6-chloropyrimidines (mezilamine, UK 177) on *in vivo* binding of labeled spiroperidol was studied in various rat brain regions. Since these neuroleptics of various chemical classes were able to prevent selective retention of spiroperidol in the striatum and tuberculum olfactorium without modifying the level in the cerebellum, it has been assumed that (3H)spiroperidol is a suitable ligand to label dopaminergic receptors in the living animal. All the neuroleptics, except the benzamides, were able to displace spiroperidol from its receptors in the frontal cortex, suggesting a serotonergic component in neuroleptic binding sites. Classical neuroleptics (haloperidol, chlorpromazine, UK 177) or atypical neuroleptics (clozapine, sulpiride, isosulpiride, mezilamine) did not induce an elective blockade of dopaminergic receptors in the striatum or in the limbic system, respectively. Results indicate that there is no correlation between the selective regional stimulation of DA turnover after neuroleptics and the *in vivo* blockade of postsynaptic dopaminergic receptors. 23 references. (Author abstract)

001364 Le Fur, Gerard; Mizoule, Jacques; Rataud, Jean; Uzan, Andre. Pharmindustrie, Groupe Pharmaka, 35, quai du Moulin de Cage, F-92231 Gennevilliers, France *Mezilamine, a new dopamine antagonist, blocks presynaptic but stimulates postsynaptic alpha-adrenoceptors*. *European Journal of Pharmacology*. 58(4):359-367, 1979.

Mezilamine, a new antidopaminergic agent, induced a concentration dependent increase in the electrically stimulated overflow of tritiated noradrenaline from male Sprague-Dawley rat cortical slices, without affecting basal overflow. The mezilamine effect on tritium overflow was antagonized by clonidine. Mezilamine also increased the electrically-induced contraction of the vas deferens, and clonidine reversed this effect. Clonidine and mezilamine both induced contractions of the rat anococcygeus muscle, whereas chlorpromazine, yohimbine, and phenoxybenzamine antagonized the anococcygeus muscle contraction induced by noradrenaline. In the pithed rat, mezilamine and clonidine increased blood pressure, but chlorpromazine and yohimbine antagonized the effects of clonidine. Mezilamine, chlorpromazine, and yohimbine also reversed the inhibitory effect of clonidine on the electrically stimulated tachycardia. Results suggest that mezilamine acts as a presynaptic alpha-antagonist and a postsynaptic alpha-agonist. 22 references. (Author abstract modified)

001365 Leach, Michael J. Dept. of Pharmacology, Wellcome Research Laboratories, Langley Court, Beckenham, Kent BR3 3BS, England *Effect of taurine on release of 3H-GABA by depolarizing stimuli from superfused slices of rat brain cerebral cortex in vitro*. *Journal of Pharmacy and Pharmacology*. 31(8):533-535, 1979.

The effect of taurine on potassium (30mM), veratrine (10 mcg ml⁻¹) and ouabain (100 mM) induced release of labelled gamma aminobutyric acid (GABA) from superfused slices of rat brain cerebral cortex was studied. Taurine (10-100mM) potentiated K-induced release of GABA but was more effective in potentiating veratrine and ouabain-induced release, and had significant effects at 5mM and 1mM respectively. The potentiation of stimulus-induced release did not appear to be due to inhibition of

reuptake and the effect is consistent with both a modulatory role and anticonvulsant action for taurine. 12 references. (Author abstract)

001366 Lee, H. K.; Chai, C. Y.; Wayner, M. J.; Kao, L. C. Dept. of Pharmacology, National Defense Medical Center, PO Box 8244, Taipei, Taiwan, Republic of China *Naloxone antagonism of electrical stimulation induced tail erection in mice*. *Pharmacology Biochemistry and Behavior*. 11(2):227-229, 1979.

Tail erection was induced by focal electrical stimulation of the mesencephalic central gray through chronically implanted electrodes in mice. The response was current intensity dependent. Pretreatment with naloxone (5mg/kg ip), a specific narcotic antagonist, abolished tail erection produced by low electrical current. In contrast, the tail response elicited by higher current was only partially blocked by naloxone. Results suggest that electrical stimulation induces tail erection by releasing an endogenous opioid peptide from the mesencephalic central gray. 17 references. (Author abstract)

001367 Lee, H. K.; Dunwiddie, T.; Hoffer, B. Hoffer: Dept. of Pharmacology, Box C236, University of Colorado Medical Center, 4200 E. Ninth Avenue, Denver, CO 80262 *Electrophysiological interactions of enkephalins with neuronal circuitry in the rat hippocampus. II. Effects on interneuron excitability*. *Brain Research*. 184(2):331-342, 1980.

The effects of active and inactive enkephalin derivatives and naloxone on putative interneurons were studied in the *in vitro* rat hippocampal slice. Inhibitory interneurons were recorded extracellularly, and identified electrophysiologically on the basis of their characteristic action potential shape and pattern of evoked firing in response to single and multiple electrical stimuli. Active enkephalin derivatives elicited a dose dependent depression in excitability whereas inactive derivatives had no effect. Naloxone reliably and reproducibly antagonized the depressant action of active enkephalins. These data confirm the hypothesis that the direct effect of enkephalins in the hippocampus is a depression of firing of inhibitory neurons, and support the hypothesis that enkephalin-induced excitations of pyramidal cells are brought about by disinhibition. 28 references. (Author abstract)

001368 Lehman, Thomas M.; Pyati, Padma; Peterson, George R. Dept. of Pharmacology, Wright State University School of Medicine, Dayton, OH 45435 *Inhibition of drug metabolism by chronically administered naltrexone*. *Life Sciences*. 25(18):1591-1600, 1979.

Naltrexone was administered to male NIH/Swiss mice via a long-term delivery system of 1.5mm beads containing 2mg naltrexone in a 90/10 polyactic/glycolic acid copolymer. A single bead implanted subcutaneously antagonized the analgesic action of intermittently administered morphine sulfate (20mg/kg i.p.) for 25 to 35 days. During this period, the activities of the hepatic microsomal mixed function oxidases aminopyrine N-demethylase and aniline hydroxylase were depressed to 30 to 50% of control levels. Hexobarbital sleeping time and zoxazolamine paralysis time were significantly prolonged, and blood half-lives of 14C-pentobarbital and 3H-amphetamine were lengthened when the monooxygenase activities were inhibited. Sleeping time after ethanol administration was not altered. *In vitro*, naltrexone and its metabolite beta-naltrexol both inhibited the activities of aminopyrine N-demethylase and aniline hydroxylase, but the parent compound was two to three times more effective than the metabolite. 36 references. (Author abstract modified)

001369 Leslie, S. W.; Friedman, M. B.; Wilcox, R. E.; Elrod, S. V. Dept. of Pharmacology, College of Pharmacy, University of Texas at Austin, Austin, TX 78712 *Acute and chronic effects*

of barbiturates on depolarization-induced calcium influx into rat synaptosomes. *Brain Research*. 185(2):409-417, 1980.

To characterize the involvement of stimulus secretion coupling in the production of CNS sedation, the development of membrane tolerance to the inhibitory actions of barbiturates on synaptosomal calcium influx during the same time frame as the occurrence of behavioral tolerance to sedation was demonstrated in rats. Depolarization induced 45Ca^{2+} influx into synaptosomes isolated from nontreated control and acutely treated rats (given 60mg/kg phenobarbital ip.) was significantly depressed by an in vitro challenge with pentobarbital. However, depolarization-induced 45Ca^{2+} influx into synaptosomes isolated from tolerant rats was not significantly altered when the synaptosomes were challenged with 0.3mM pentobarbital. It is suggested that synaptosomal membranes adapt during chronic exposure to barbiturates to allow for an enhanced Ca^{2+} influx subsequent to depolarization. It is also suggested that sedation may, at least in part, occur as a result of depressed stimulus secretion coupling and that behavioral tolerance to sedation may occur because of the development of membrane tolerance to allow enhanced calcium influx. 20 references. (Author abstract modified)

001370 Levin, Barry E. Neurology Service (127), Veterans Administration Medical Center, East Orange, NJ 07019 Effects of reserpine on fast, intermediate and slow axonal transport of proteins in rat locus coeruleus neurons. *Brain Research*. 189(2):495-504, 1980.

The effects of a single injection of reserpine on protein turnover and axonal transport (AT) in locus coeruleus (LC) noradrenergic neurons was investigated in the rat. Reserpine pretreatment, at intervals of 1 to 21 days prior to (3H)fucose or leucine injections into the LC, resulted in marked alterations in the turnover of (3H) glycoproteins and proteins in the LC and hypothalamus which were present for up to 14 days and varied according to the time after reserpine pretreatment. Reserpine produced an intermittent blockade, of variable degree, in rapidly and intermediately transported proteins for up to 2 weeks following injection. Slow AT was uniformly decreased over the first 10 posttreatment days to 2% to 42% of controls. Blockade and not a change in the rate or time of onset of transport appeared to be responsible for the observed changes. The suggested mechanisms for these alterations is a reordering of metabolic priorities in the synthesis and transport of proteins in these noradrenergic cells secondary to a reserpine-induced depletion of norepinephrine in the nerve terminals. 27 references. (Author abstract)

001371 Levin, R. M.; Weiss, B. Dept. of Pharmacology, Medical College of Pennsylvania, 3300 Henry Avenue, Philadelphia, PA 19129 Inhibition by trifluoperazine of calmodulin-induced activation of ATPase activity of rat erythrocyte. *Neuropharmacology*. 19(2):169-174, 1980.

An endogenous, heat stable, calcium binding protein (calmodulin), which was previously shown to increase the activity of one of the forms of cyclic nucleotide phosphodiesterase, was found to increase selectively the activity of a (Ca^{2+} plus Mg^{2+})-ATPase of rat erythrocyte membranes. The ED_{50} for calmodulin activation was 150ng calmodulin/ml. The concentration of Ca^{2+} required for half maximum calmodulin-induced activation of erythrocyte ATPase was 20microM whereas approximately 50microM Ca^{2+} was required for half maximum calcium-induced activation of ATPase measured in the absence of calmodulin. The phenothiazine trifluoperazine, which specifically inhibits the activation of phosphodiesterase by high affinity, calcium specific binding to calmodulin, specifically inhibited the calmodulin-induced activation of ATPase; the I_{50} for inhibition of ATPase was 50microM when measured in the presence of calmodulin

but was over 250microM when measured in its absence. The trifluoperazine-induced inhibition of ATPase could be overcome by adding excess calmodulin. Results indicate that calmodulin activates a specific form of erythrocyte ATPase and that trifluoperazine selectively inhibits this activation presumably by binding to calmodulin. Results further support the hypothesis that several of the biochemical actions of phenothiazine antipsychotics can be explained by a common mechanism, namely, by selectively binding to calmodulin and thereby inhibiting its action. 29 references. (Author abstract modified)

001372 Levy, Lewis; Wicke, J. D. Neurology Service/127, Veterans Administration Medical Center, West Spring Street, West Haven, CT 06516 The effect of alpha-adrenergic innervation on caudate blood flow. *Annals of Neurology*. 7(2):150-156, 1980.

A thermal diffusion probe, with cannulae for intracerebral microinfusion of drugs and an electrode to monitor EEG activity, was used to examine the local effect of vasoactive amines in a 4 to 5 mm sphere of caudate nucleus in cats. Results demonstrate that it is possible to alter local cerebral blood flow (CBF) without causing any change in systemic blood pressure or heart rate, or in CBF and the EEG in the opposite caudate. One mcl intracerebral injections, containing varying amounts of phenylephrine, increased local CBF in proportion to dose. The effect was blocked by intracerebral infusion of phentolamine. However, local alpha-adrenergic blockade did not inhibit vascular responses to blood pressure elevation or to metabolic influences on local blood flow. 26 references. (Author abstract)

001373 Lien, E. L.; Morrison, A.; Dvornich, William. Wyeth Laboratories, Inc., P.O. Box 8299, Philadelphia, PA 19101 The effects of partial opiate agonists on plasma prolactin and growth hormone levels in the rat. *Life Sciences*. 25(20):1709-1715, 1979.

Opiate agonists, partial agonists, and antagonists differed in their effects on the release of growth hormone and prolactin in male CD rats. The agonists morphine, methadone, and meperidine elevated plasma levels of both hormones. Naloxone, an opiate antagonist, lowered levels of prolactin but not of growth hormone. All partial agonists studied raised growth hormone levels; among these, levallorphan, nalorphine, and ciramadol lowered prolactin levels, but pentazocine and meptazinol did not. Naloxone blocked the morphine-induced release of prolactin and growth hormone. The partial agonists suppressed morphine-induced prolactin release, and several also suppressed the elevation of growth hormone levels. Comparison of these findings with results from the opiate radioreceptor assay suggest that opioid compounds can be classified as agonists, antagonists, or partial agonists on the basis of their effects on prolactin and growth hormone release. 21 references. (Author abstract modified)

001374 Lindeke, Bjorn; Paulsen, Ulla; Anderson, Elisabet. Dept. of Organic Pharmaceutical Chemistry, Biomedical Center, University of Uppsala, Box 574, S-751 23, Uppsala, Sweden Cytochrome P-455 complex formation in the metabolism of phenylalkylamines -- IV. Spectral evidences for metabolic conversion of methamphetamine to N-hydroxymphetamine. *Biochemical Pharmacology*. 28(24):3629-3635, 1979.

Liver microsomes from phenobarbital treated rats were incubated with N-methylamphetamine (1) and its N-oxidized congeners N-hydroxy-N-methylamphetamine (2), N-methylene-1-phenyl-2-propylamine N-oxide (3a), N-(1-phenyl-2-propylidene)methylamine N-oxide (3b), N-hydroxymphetamine (4a), and N-hydroxymethylamine (4b). Incubation with compounds 1, 2, 3a, and 3b gave rise to the formation of cytochrome P-450 product complexes characterized by maximum absorbances in the 453 to 457 nm region. Compounds 1, 2, and 3a

showed maximum absorbances at 456 nm; and for 2 and 3a, both the rate and extent of complex formation was increased several fold over those of 1, with the complexing activity being about 90% of that of 4a. Contrary to 1, 2, 3a, and 4a, nitro compound 3b showed its maximum absorbance at 453 nm and the spectral perturbations were identical to those shown with 4b. Demethylation of 1 and 2 showed good correlation with the complex formation. Data indicate that 3a, formed after metabolic N-oxidation of 1, undergoes further conversion to 4a, the latter being the ultimate precursor to the ligand forming the cytochrome P-455 complex. Results substantiate the notion that there is a preference for the formation of nitrones related to 3a rather than 3b during the metabolism of N-alkylamphetamines. 26 references. (Author abstract modified)

001375 Lockton, J. W.; Holmes, O. Holmes: Institute of Physiology, University of Glasgow, Glasgow G12 8QQ, Scotland **Site of the initiation of penicillin-induced epilepsy in the cortex cerebri of the rat.** *Brain Research.* 190(1):301-304, 1980.

The site of initiation of penicillin-induced epilepsy in the cortex cerebri of the rat was investigated using the technique established by Walsh of applying penicillin electrophoretically from a glass micropipette inserted into the cortex. Although with small doses of the penicillin the 0.5 to 0.8 mm zone appears to be the zone in which epileptic spikes are triggered, the responses to larger doses of penicillin demonstrate that many zones of cortex, if sufficiently excited, are capable of generating epileptic spikes. It is concluded that on the basis of present evidence, the sensitive region of the cortex can be localized as lying within laminae III to V. 5 references.

001376 Lodge, D.; Curtis, D. R.; Johnston, G. A. R.; Bornstein, J. C. Curtis: Dept. of Pharmacology, John Curtin School of Medical Research, P. O. Box 334, Canberra City, A. C. T., 2601, Australia **In vivo inactivation of quisqualate: studies in the cat spinal cord.** *Brain Research.* 182(2):491-495, 1980.

The excitatory effects of quisqualate and other amino acids were compared on dorsal horn interneurons and Renshaw cells in lumbar segments of anesthetized spinal cats. The time course of onset and recovery of quisqualate was similar to those of L-glutamate, D-glutamate, and L-homocysteate and faster than those of D-homocysteate, N-methyl-D-aspartate, and kainate. Dihydrokainate and threo-3-hydroxy-D-aspartate, which inhibit high affinity uptake of L-glutamate in vitro, enhanced the in vivo excitatory action of glutamate and quisqualate. Results suggest that quisqualate is removed from the extracellular environment by uptake systems that also transport L-glutamate and other amino acids. 16 references.

001377 Loewy, A. D.; McKellar, S.; Swenson, E. E.; Panetton, W. M. Dept. of Anatomy and Neurobiology, Washington University School of Medicine, St. Louis, MO 63110 **Onset of hypertension in spontaneously hypertensive rats despite the depletion of spinal cord catecholamines.** *Brain Research.* 185(2):449-454, 1980.

The possible role of the spinal catecholamine systems in the development of spontaneously hypertensive (SHR) hypertension was examined in the rat using anatomical techniques to document the effects of 6-hydroxydopamine (6-OHDA). Results indicate that descending noradrenergic fiber systems do not trigger the onset of hypertension in the SHR model. Intraventricular injections of 6-OHDA delayed, but did not completely prevent the onset of hypertension in SHR rats. It is suggested that the early onset may be central in origin, while the later onset may be a separate abnormality. It is concluded that the early onset of hypertension in the SHR rat does not require the integrity of

spinal catecholamine systems, but the relevant system affected by 6-OHDA must lie in the brain. 19 references.

001378 Logan, J. G. Dept. of Physiology, London Hospital Medical College, Turner Street, London E1 2AD, England **In vitro effects of lithium chloride on ATPases of rabbit cerebral synaptic membranes.** *Biochemical Pharmacology.* 29(6):887-889, 1980.

The in vitro effects of lithium on the ATPase of rabbit cerebral synaptic membranes were investigated under conditions designed to manipulate the specific activity of the enzymes. Lithium chloride (3mM) stimulated Mg ATPase and inhibited (Na-K) ATPase of rabbit cerebral synaptic membranes. The inhibitory effects of lithium were dependent on the ionic strength of the incubation medium. Lithium increased the activation energies of Mg ATPase and (Na-K) ATPase. The results are not consistent with the model of the therapeutic effects of lithium proposed by previous studies. 25 references. (Author abstract modified)

001379 Logan, J. G.; O'Donovan, D. J. Dept. of Physiology, London Hospital Medical College, Turner Street, London E1 2AD, England **The effect of desipramine on the noradrenaline stimulated Na-K ATPase of rabbit synaptic membranes.** *Biochemical Pharmacology.* 29(1):111-112, 1980.

The effects of inhibitors of noradrenaline uptake (phentolamine, chlorpromazine, desipramine, and imipramine) on the noradrenaline stimulation of Na-K ATPase were investigated in albino rabbits. Results indicate that the activation of Na-K ATPase by noradrenaline was antagonized by phentolamine more than chlorpromazine, and by chlorpromazine more than desipramine. Phentolamine was a competitive antagonist and desipramine was a noncompetitive antagonist of the noradrenaline effect on the enzyme. 11 references.

001380 Logan, William J.; Swanson, James M. Division of Neurology, Hospital for Sick Children, Toronto, Ontario, Canada M5G 1X8 **Erythrosin B inhibition of neurotransmitter accumulation by rat brain homogenate.** *Science.* 206(4416):363-364, 1979.

The effects of erythrosin B on neurotransmitter accumulation in rat brain homogenate were investigated in relation to hypothesized behavioral abnormalities following ingestion of food dyes. A mixture of seven food dyes inhibited the accumulation of eight neurotransmitters or neurotransmitter precursors by rat brain homogenate. At a low concentration (1 mcg per ml), erythrosin B (FD & C red 3) was the only dye that inhibited dopamine accumulation. Erythrosin also was effective in decreasing the accumulation of all the other transmitter substances, suggesting that the inhibition is nonspecific and probably secondary to general membrane alteration. 5 references. (Author abstract modified)

001381 Login, Ivan S.; Macleod, Robert M. Dept. of Neurology, University of Virginia School of Medicine, Charlottesville, VA 22908 **Failure of opiates to reverse dopamine inhibition of prolactin secretion in vitro.** *European Journal of Pharmacology.* 60(2/3):253-255, 1979.

To identify the site of action of opiate-induced prolactin elevation, in vitro female Sprague-Dawley rat hemipituitary incubations were performed in the presence of morphine, met-enkephalin, ala2-met5-enkephalinamide, dopamine (DA), or opiate/DA combinations. No opiate stimulated prolactin release directly or blocked the inhibitory effect of DA. It is concluded that this opiate endocrine action is not mediated at the pituitary level, but may involve interference with hypothalamic DA release. 11 references. (Author abstract modified)

001382 Lorden, Joan F. Dept. of Psychology, University of Alabama, University Station, Birmingham, AL 35294 **Differential effects on body weight of central 6-hydroxydopamine lesions in obese (ob/ob) and diabetes (db/db) mice.** *Journal of Comparative and Physiological Psychology.* 93(6):1085-1096, 1979.

Because the catecholamines, and particularly norepinephrine (NE), are implicated in the control of feeding, levels of central catecholamines were experimentally reduced in obese (ob/ob) and diabetes (db/db) mice to investigate the role of the catecholamines in these cases of spontaneously occurring obesity. Lesions produced by 6-hydroxydopamine (6-OHDA) were used to produce large depletions of NE and dopamine (DA). In the db/db but not the ob/ob, central catecholamine depletion was accompanied by a significant and persistent weight loss and by a reduction in plasma glucose levels when compared with vehicle infused controls. It is concluded that abnormalities in central noradrenergic systems may account for part of the obesity syndrome observed in the diabetes mouse. 53 references. (Author abstract modified)

001383 Lueders, H.; Bustamante, L.; Zablow, L.; Krinsky, A.; Goldensohn, E. S. Dept. of Neurology, College of Physicians and Surgeons, Columbia University, New York, NY 10032 **Quantitative studies of spike foci induced by minimal concentrations of penicillin.** *Electroencephalography and Clinical Neurophysiology.* 48(1):80-89, 1980.

An attempt was made to provide a sensitive and stable spike focus model for quantitative evaluation of the effects of anticonvulsants on the characteristics of the primary spike focus and on afterdischarges. Interrelationships in spike latency, spike amplitude, amplitude of prepositivity, spike duration, and spike frequency were also examined. The minimum concentration of penicillin required to induce stable recurrent spikes (20,000U/ml) and to elicit stable recurrent afterdischarges (100,000U/ml) were determined in cats. 15 references.

001384 Lykouras, Eleftherios; Eccleston, Donald; Marshall, Elizabeth F. Dept. of Psychiatry, University of Newcastle-upon-Tyne, Newcastle-upon-Tyne, NE1 4LP, England **The effect of a 5HT agonist on cyclic guanosine monophosphate in rat cerebellum.** *Biochemical Pharmacology.* 29(5):827-828, 1980.

The possibility that changes in 5-hydroxytryptamine (5-HT) metabolism may be reflected in changes in cerebellar cyclic guanosine monophosphate (cGMP) concentrations was investigated by determining the effect of 5-methoxy-dimethyl-tryptamine (5MeODMT), a suggested 5-HT agonist, on the concentration of cGMP in rat cerebellum. Results indicate that a 5-HT-like agonist can elicit an increase in cGMP in the cerebellum. This increase is of the same order as that found after apomorphine, but the lack of effect of haloperidol on the 5MeODMT stimulated increase in cGMP indicates, however, the existence of a neuronal pathway which overrides dopaminergic activity. Data indicate that the concentration of cerebellar cGMP may be controlled by a 5-HT mediated pathway which is not blocked by cyproheptadine or methysergide, and which does not appear to require the activation of an intermediate dopaminergic neuron. 17 references.

001385 Maas, James W.; Hattox, Susan E.; Landis, D. Harold. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Differential effects on brain catecholamines by debrisoquin.** *Biochemical Pharmacology.* 28(20):3153-3156, 1979.

The effects of debrisoquin on brain norepinephrine (NE) and dopamine (DA) were determined by measuring levels of the metabolites 3-methoxy-4-hydroxyphenylglycol (MHPG) and homovanillic acid (HVA) before and during treatment of Macaca arcoides with debrisoquin for 1 week. Results showed the MHPG

output was significantly reduced by debrisoquin, while HVA was not significantly altered. This finding indicates that debrisoquin does not act directly via inhibition of monoamine oxidase in the CNS and suggests it may be useful in pharmacological studies in which a differentiation between NE and DA effects is desired. 10 references.

001386 MacDonald, J. Ferguson; Barker, Jeffery L.; Paul, Steven M.; Marangos, Paul J.; Skolnick, Philip. Laboratory of Neurophysiology, National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, MD 20205 **Inosine may be an endogenous ligand for benzodiazepine receptors on cultured spinal neurons.** *Science.* 205(4407):715-717, 1979.

Mouse spinal neurons grown in tissue culture were used to study the membrane effects of the benzodiazepine flurazepam and the naturally occurring purine nucleoside inosine, which competes for benzodiazepine receptor sites in the central nervous system. Application of inosine elicited two types of transmitter-like membrane effects: a rapidly desensitizing excitatory response and a nonsensitizing inhibitory response. Flurazepam produced a similar excitatory response which showed cross-desensitization with the purine excitation. Flurazepam also blocked the inhibitory inosine response. Results provide electrophysiological evidence that an endogenous purine can activate two different conductances on spinal neurons and that flurazepam can activate one of the conductances and antagonize the other. 19 references. (Author abstract)

001387 Macmillan, V. Dept. of Medicine, University of Toronto, Toronto, M5S 1A8, Canada **Sequential alterations of cerebral carbohydrate metabolism associated with gamma-hydroxybutyrate.** *Brain Research.* 183(1):123-134, 1980.

Cerebral contents of selected glycolytic/citric acid cycle intermediates and energy phosphates were measured following i.v. injection of 1000mg/kg gamma-hydroxybutyrate (GHB) to lightly anesthetized male Wistar rats. The initial change in the glycolytic pathway occurred within 2.5 minutes, with increases of tissue glucose-6-phosphate and decreases of fructose-1,6-diphosphate indicating an inhibition of phosphofructokinase. Within 5 to 15 minutes of GHB injection, increasing tissue glucose and decreasing glucose-6-phosphate were observed, indicating inhibition of hexokinase. The initial inhibition of phosphofructokinase was associated with functional depression, an isoelectric EEG, and an increase in tissue phosphocreatine. Within 2.5 minutes of GHB injection, tissue-alpha-ketoglutarate and aspartate showed significant increases, suggesting a shift in the aspartate aminotransferase reaction. GHB did not alter the cytoplasmic redox state. 32 references. (Author abstract modified)

001388 MacVicar, Brian A.; Dudek, F. Edward. Dept. of Zoology, Erindale College, University of Toronto, Mississauga, Ontario L5L 1C6, Canada **Local synaptic circuits in rat hippocampus: interactions between pyramidal cells.** *Brain Research.* 184(1):220-223, 1980.

The local synaptic interactions of CA3 pyramidal cells were examined with simultaneous intracellular recordings in slices of rat hippocampus. After obtaining two simultaneous intracellular impalements, action potentials were evoked by intracellularly injected current to determine whether synaptic connections existed between the pyramidal cells. In 10 out of over 88 pairs of cells, spikes in one cell resulted in inhibition of the other cell. These results demonstrate the dual effect spikes in one pyramidal cell can have on other pyramidal cells in the same subfield. It is suggested that the CA3 region is not merely a point transferring information through the hippocampus but that substantial processing may be occurring in the subfield. 18 references.

001389 Maekawa, Tsuyoshi; Oshibuchi, Takao; Imamura, Akihisa; Takeshita, Hiroshi. Dept. of Anesthesiology, Yamaguchi University, School of Medicine, 1144 Kogushi, Ube, Yamaguchi, Japan. Effects of psychotropic drugs on the cerebral energy state and glycolytic metabolism in the rat: diazepam, clomipramine and chlorpromazine. *Biochemical Pharmacology*. 29(1):15-18, 1980.

The effects of psychotropic drugs (diazepam, clomipramine, and chlorpromazine) on the central energy state and glycolytic metabolism in the rat were investigated. Phosphocreatine, adenosine 5'-triphosphate, adenosine diphosphate, adenosine monophosphate, glucose, glucose-6-phosphate, lactate, and pyruvate were measured with the cerebral cortex tissues frozen in situ by liquid nitrogen after the intravenous administration of the drugs. There were no significant changes in the levels of cerebral high energy phosphates or energy charge potential. There were also no significant changes in the levels of glycolytic intermediates or the lactate/pyruvate ratio (L/P ratio), except for an increase in glucose after the administration of chlorpromazine. Thus, none of these drugs appeared to impede the cerebral energy state in a therapeutic dose. 15 references. (Author abstract modified)

001390 Maggi, A.; Enna, S. J. Enna: Dept. of Neurobiology and Anatomy, University of Texas Medical School, P.O. Box 20708, Houston, TX 77025. Regional alterations in rat brain neurotransmitter systems following chronic lithium treatment. *Journal of Neurochemistry*. 34(4):888-892, 1980.

Lithium was administered chronically to rats by way of their diet at a dose sufficient to maintain a blood level similar to that found to be clinically effective. A separate group of animals received rubidium, an ion postulated to be effective in treating the depression associated with manic-depressive psychosis. Following treatment, the receptor binding characteristics of the serotonergic, cholinergic muscarinic, beta-adrenergic, and GABAergic systems were studied in various brain regions, in addition to dopamine turnover in the corpus striatum. Results suggest that, under these conditions, lithium, but not rubidium, can selectively affect serotonin and GABA receptor binding in specific brain areas, and appears to increase the synaptic concentration of dopamine in the corpus striatum. 15 references. (Author abstract modified)

001391 Maher, Timothy J.; Wurtman, Richard J. Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139. L-threonine administration increases glycine concentrations in the rat central nervous system. *Life Sciences*. 26(16):1283-1286, 1980.

Intraperitoneal administration of L-threonine increased the glycine and threonine concentrations in rat spinal cord. Glycine contents also increased in synaptosomes prepared from spinal cords from threonine pretreated animals. These findings suggest that plasma threonine concentrations normally might affect production of glycine by central nervous system neurons, and also that exogenous threonine might be useful in modifying glycinergic transmission. 23 references. (Author abstract)

001392 Mallorga, Pierre; Hamburg, Margaret; Tallman, John F.; Gallagher, Dorothy W. Section on Biochemistry and Pharmacology, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205. Ontogenetic changes in GABA modulation of brain benzodiazepine binding. *Neuropharmacology*. 19(4):405-408, 1980.

The ontogenesis of the (3H)diazepam binding sites and their modulation by GABA was investigated in the rat cortex. Specific binding of (3H)diazepam (calculated in fmole per mcg of wet weight of tissue) is 2% of adult binding level, when measured at

16 days of gestation, 20% at birth, and reaches the adult levels approximately 3 weeks after birth. An increase in (3H)diazepam binding after the in vitro addition of GABA to the extensively washed rat brain membrane preparation was observed at each stage of development and was due to a change in affinity without significant alteration in the total number of (3H)diazepam binding sites. Furthermore, the GABA effect was found to decrease with age. 12 references. (Author abstract)

001393 Malseed, Roger T.; Goldstein, Frederick J. Dept. of Biological Sciences, Philadelphia College of Pharmacy and Science, 43rd St. and Kingsessing Mall, Philadelphia, PA 19104. Enhancement of morphine analgesia by tricyclic antidepressants. *Neuropharmacology*. 18(10):827-829, 1979.

The antinociceptive action of subcutaneous morphine (0.25mg/kg) in cats was enhanced by pretreatment with 10mg/kg subcutaneous amitriptyline or nortriptyline. No analgesia was observed following subcutaneous administration of either tricyclic antidepressant alone. The augmentation of morphine analgesia by tricyclic antidepressants may be related to both central and peripheral actions of the drugs. 11 references. (Author abstract modified)

001394 Mansour, Tag E.; Mansour, Joan M. Dept. of Pharmacology, Stanford University School of Medicine, Stanford, CA 94305. Effect of some phosphodiesterase inhibitors on adenylate cyclase from the liver fluke, *Fasciola hepatica*. *Biochemical Pharmacology*. 28(12):1943-1946, 1979.

Serotonin (5-HT) activated adenylate cyclase from particulate fractions of the liver fluke was inhibited by papaverine, 1-ethyl-4-(isopropylidenehydrazino)-1H-pyrazolo-(3,4-b)-pyridine-5-carboxylic acid, (SQ-20009), 6,7-dimethyl-4-ethyl-quinazoline, and caffeine. This inhibition may account for the ability of these phosphodiesterase inhibitors to antagonize the 5-HT mediated rise in endogenous cyclic AMP levels in vivo. Isobutylmethylxanthine, which does not antagonize the 5-HT effect in vivo, did not inhibit 5-HT activated adenylate cyclase in fluke particles. None of the compounds tested inhibited the sodium fluoride activated adenylate cyclase. Kinetic studies showed that inhibition of 5-HT activated adenylate cyclase by papaverine or SQ-20009 was not competitive with substrate, ATP, or guanosine triphosphate. High levels of 5-HT decreased the degree of inhibition by papaverine or SQ-20009, but the kinetics of inhibition did not appear to be strictly competitive. 15 references. (Author abstract modified)

001395 Manukhin, Boris N.; Volina, Ekaterina V. N. K. Koltzov, Institute of Developmental Biology, USSR Academy of Sciences, Vavilov St. 26, 117334, Moscow, USSR. Reverse transsynaptic regulation of neuronal noradrenaline uptake. *Biochemical Pharmacology*. 28(13):2037-2044, 1979.

The beta-adrenergic antagonist propranolol activated uptake of tritiated noradrenaline (NA) by isolated rat organs by 30 to 180%, while the alpha-adrenergic antagonist phentolamine activated NA uptake (by 30 to 50%) only in organs with postsynaptic alpha-adrenoceptors (vas deferens, spleen, and small intestine). The beta-adrenoceptor agonist isopropylnoradrenaline decreased (3H)NA uptake by 15 to 50% in all organs studied; alpha-adrenergic stimulants urea and mesatone inhibited (3H)NA uptake by 20 to 45% in organs with postsynaptic alpha-adrenoceptors. The activation of neuronal (3H)NA uptake induced by phentolamine was due to release of a humoral factor from the effector cell and its influence on adrenergic neurons. Mesatone caused the formation and release of a humoral factor inhibiting neuronal (3H)NA uptake. The possible mechanism of the reverse transsynaptic regulation of neuronal NA

uptake via the adrenoceptors of the effector cell is discussed. 37 references. (Author abstract modified)

001396 Marangos, Paul J.; Clark, Reena; Martino, Andrea M.; Paul, Steven M.; Skolnick, Phil. CPB/NIMH, Building 10, Room 4S239, 9000 Rockville Pike, Bethesda, MD 20205 **Demonstration of two new endogenous compounds from brain.** Psychiatry Research. 1(2):121-130, 1979.

The nature and identity of possible endogenous ligands for the benzodiazepine receptor in the brain was studied using bovine and rat tissue. Two previously undescribed fractions capable of apparent competitive inhibition of (3H)diazepam binding were found. Both factors are heat stable and resistant to proteolytic degradation. The larger factor (approximately 700 to 30,000 daltons) is found in pituitary, liver, and muscle, but the highest levels are found in brain. 9 references. (Author abstract modified)

001397 Marchais, D.; Tassin, J. P.; Bockaert, J. Laboratoire de Physiologie Cellulaire, Collège de France, 11 place Marcelin Berthelot, F-75231 Paris, France **Dopaminergic component of (3H)spiroperidol binding in the rat anterior cerebral cortex.** Brain Research. 183(1):235-240, 1980.

The binding of tritiated spiroperidol in rat frontal cortex (Fc) was examined. Results showed that (3H)spiroperidol binds to dopamine (DA) receptors in Fc similar to those in corpus striatum, with high affinities for DA and DA analogues. These receptors probably do not constitute a homogenous population, but are distinct from the DA receptors coupled with adenylate cyclase and from those that show a higher affinity for serotonin than for DA. 13 references.

001398 Martin, Gregory E.; Bacino, Charlotte B. Merck Institute for Therapeutic Research, West Point, PA 19486 **Action of intracerebrally injected beta-endorphin on the rat's core temperature.** European Journal of Pharmacology. 59(3/4):227-236, 1979.

When microinjected directly into the preoptic anterior hypothalamus, beta-endorphin (0.74 to 7.4 nmol) induced an increase in rectal temperature (RT) in freely moving male Sprague-Dawley rats. The initial phase of the endorphin-induced rise in RT was partially attenuated by naloxone (5 or 20 mg/kg i.p.) or naltrexone (3 mg/kg i.p.), and the late phase was completely blocked by the prostaglandin synthesis inhibitor indomethacin (15 mg/kg i.p.). Pretreatment with indomethacin in combination with naloxone resulted in a near total block of the endorphin-induced increase in RT. Endorphin evoked fever was also antagonized by methergoline (1 mg/kg i.p.), suggesting that serotonin mediates the rise in RT. When beta-endorphin was injected into the lateral cerebral ventricle, catalepsy, analgesia, and marked drop in RT were observed; these effects were completely blocked by naloxone. Beta-endorphin elicited naloxone reversible hyperthermia when injected into the subarachnoid space surrounding the spinal cord. 27 references. (Author abstract modified)

001399 Martin, I. L.; Candy, J. M. MRC Neuropharmacology Unit, Medical School, Birmingham B15 2TJ, England **Facilitation of specific benzodiazepine binding in rat brain membrane fragments by a number of anions.** Neuropharmacology. 19(2):175-179, 1980.

The ability of eight anions, in the concentration range 0 mM to 200 mM, to facilitate specific (3H)-diazepam binding to well washed membrane fragments prepared from whole rat brain (less medulla/pons) was investigated. All the anions studied produced a significant increase in specific (3H)-diazepam binding, though to different degrees, with the exception of isethionate which showed no effect at any concentration investigated. Scat-

chard analysis revealed that Br⁻ (50 mM) produced a significant increase in the affinity of the receptor for (3H)-diazepam with no change in the total number of sites available, and that with the additional presence of GABA (10 μM), the affinity was further increased again with no changes in the number of sites available. Attempts to correlate the facilitatory effects of these anions on specific (3H)-diazepam binding with their ability to modify cortical inhibitory postsynaptic potentials which are thought to be chloride mediated produced no significant correlation; neither was there an obvious correlation between the facilitatory effects of these anions and their chaotropic properties. The facilitatory effects of these anions on specific (3H)-diazepam binding cannot be explained adequately either by an intimate linkage between the benzodiazepine receptor and a chloride channel nor by the chaotropic properties of these anions alone. 21 references. (Author abstract)

001400 Martinet, M.; Fonlupt, P.; Pacheco, H. Service de Chimie Biologique, Bat 406, I.N.S.A. 20 Avenue Albert Einstein, F-69621 Villeurbanne CEDEX, France **Effects of cytidine-5' diphosphocholine on norepinephrine, dopamine and serotonin synthesis in various regions of the rat brain.** Archives Internationales de Pharmacodynamie et de Therapie. 239(1):52-61, 1979.

Intravenously administered cytidine-5' diphosphocholine significantly increased tyrosine and dopamine levels and the dopamine synthesis rate in the male Wistar rat corpus striatum, with maximum effect at 50 mg/kg 1 hour after administration. The nucleotide also decreased the level of serotonin and tryptophan and the rate of serotonin synthesis in the midbrain/hypothalamus and in the brainstem. The increase in striatal dopamine level and the decrease in brainstem and midbrain serotonin level are correlated with the antiparkinson and neurostimulant action of the nucleotide. 23 references. (Author abstract modified)

001401 Marzi, Adriana; de Toranzo, Edith G. D.; Castro, Jose A. Laboratorio de Quimica Biotoxicologica, CITEFA, Zufriategui y Varela, Villa Martelli, Pcia de Buenos Aires, Argentina **Mechanism of chlorpromazine prevention of carbon tetrachloride-induced liver necrosis.** Toxicology and Applied Pharmacology. 52(1):82-88, 1980.

The mechanism of chlorpromazine (CPZ) prevention of carbon tetrachloride (CCl₄) induced liver necrosis was examined in the rat. CPZ was able to partially prevent liver necrosis in rats 24 hr but not 72 hr after CCl₄ administration. Preventive effects at 24 hr were still observed when CPZ was given as much as 10 hr after CCl₄. Prevention was not due to variation in CCl₄ concentration in liver. CPZ did not decrease either the covalent binding of CCl₄ reactive metabolites to cellular constituents or lipid peroxidation, but caused a marked decrease in body temperature. Results indicate that CPZ only delays onset of hepatotoxicity, and suggest that this effect is mediated by the CPZ effect on body temperature, as necrosis observed in CPZ treated animals injected with CCl₄ and maintained at 37 degrees C was as intense as that observed in animals receiving CCl₄ alone. (Author abstract modified)

001402 Masana, M. I.; Rubio, M. C. Instituto de Investigaciones Farmacologicas, CONICET, Junin 956 - 5 Piso, 1113, Buenos Aires, Argentina **Modulatory role of catecholamines on tyrosine hydroxylase induction.** Naunyn-Schmiedeberg's Archives of Pharmacology. 308(1):25-29, 1979.

The modulatory role of cytoplasmic catecholamines on tyrosine hydroxylase (TH) induction was studied in female rat superior cervical ganglia in organ culture. Exposure to carbachol almost doubled TH activity, but incubation with noradrenaline or dopamine impaired the carbachol mediated induction of the

enzyme. This effect was not blocked by propranolol, haloperidol, or phenolamine. Inhibition of monoamine oxidase activity with pargyline inhibited the effect of carbachol. Carbachol induced TH in ganglia treated with alpha-methyl-p-tyrosine to deplete endogenous catecholamines to the same extent as in normal ganglia. It is suggested that the long-term regulation of TH is modulated by a strategic cytoplasmic pool of catecholamines. 23 references. (Author abstract modified)

001403 Massotti, M.; Guidotti, A.; Schmid, R.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Endogenous inhibitors of Na independent 3H-GABA binding to crude synaptic membranes.** (Unpublished paper). Washington, DC, NIMH, 1979. 28 p.

The content of GABA and other amino acids, the amount of endogenous inhibitors of 3H-GABA binding, and the kinetic characteristics of 3H-GABA binding to crude synaptic membrane preparations obtained from different rat brain areas were determined. The chemical nature, the content, and the degree of molecular heterogeneity of the endogenous substances which interfere with the binding of 3H-GABA are shown to vary considerably depending on the brain area studied and on the method used to prepare the synaptic membranes. Standardized procedural guidelines to prepare membranes practically devoid of endogenous inhibitors of GABA binding are reported, and the nature of various inhibitor materials and the kinetic characteristics and number of postsynaptic GABA receptors in various areas of the rat brain are discussed. 18 references. (Author abstract modified)

001404 Math, F.; Davrainville, J. L. Davrainville: Laboratoire de Physiologie Generale II, Université de Nancy I, C.O. 140, F-54037 Nancy Cedex, France **Electrophysiological study on the postnatal development of mitral cell activity in the rat olfactory bulb.** Brain Research. 190(1):243-247, 1980.

Postnatal evolution of recurrent inhibition which follows intense electrical stimulation of the rat contralateral olfactory bulb is examined and the action of calcium ions on this evolution is considered. Activity of the olfactory bulb underwent changes during the early postnatal period; increased spontaneous mitral cell activity was found; inhibition in response to high frequency stimulation of the contralateral bulb was detectable from birth, reduced to a minimum around the third day and intensified after 7 days; and low frequency stimulation evoked action potentials with long latencies during the first week, thereafter it became increasingly difficult to elicit. These results suggest a precocious maturation of the excitatory pathways during the first postnatal week; thereafter, an inhibitory system originating in granule cells becomes predominant. Calcium is demonstrated to modify the characteristics of mitral cell activity, a neuronal activation being observed at low levels whereas high doses cause inactivation. Cell sensitivity to calcium effect increases during the development period. These modifications may be explained by structural modifications of the cell membrane as well as by differences in the nature and level of neurotransmitters. 11 references.

001405 Matsutani, T.; Nagayoshi, M.; Tamaru, M.; Tsukada, Y. Dept. of Dev. Physiology, Inst. for Comprehensive Medical Sciences, Fujita-Gakuen University, School of Med., Toyoake, Aichi 470-11, Japan **Elevated monoamine levels in the cerebral hemispheres of microencephalic rats treated prenatally with methylazoxymethanol or cytosine arabinoside.** Journal of Neurochemistry. 34(4):950-956, 1980.

Prolonged neurochemical change and the increase of monoamines in the cerebral hemispheres of rats treated prenatally with methylazoxymethanol (MAM) or cytosine arabinoside (ara-C)

were studied. MAM injection to rats on day 15 of gestation caused a significant rise in monoamine concentrations accompanying a decrease in the brain weight and DNA content in the cerebral hemispheres of the offspring at 3 months of age; in the brainstem these changes were much smaller. Similar changes of monoamine concentrations were observed in ara-C-induced microencephaly. Although the marked decrease of DNA content in the cerebral hemispheres of MAM treated rats indicates a loss of cerebral cells due to prenatal MAM poisoning, the kind of cells destroyed remain to be studied. Normal activity of CNPase suggested that the remaining neurons, axons, and oligodendroglia were intact. 50 references. (Author abstract modified)

001406 Mattsson, Hillevi. Dept. of Pharmacology, AB Hassle, Fack, S-431 20 Molndal, Sweden **Bicyclic phosphates increase the cyclic GMP level in rat cerebellum, presumably due to reduced GABA inhibition.** Brain Research. 181(1):175-184, 1980.

Isopropyl bicyclic phosphate (IPTBO, 0.06mg/kg i.p.) produced a fourfold increase in the cyclic guanosine monophosphate (GMP) content of Wistar rat cerebellar cortex. This increase was not antagonized by pretreatment with the nicotinamide antagonist 3-acetylpyridine (65mg/kg i.p.), which destroys climbing fibers. However, GABA (15mmol intraventricularly) and muscimol (3 or 10mmol i.p.) abated the IPTBO-induced increase in cyclic GMP. IPTBO blocked the binding of dihydropicrotoxin to brain membranes, but did not alter the sodium independent receptor binding of GABA to synaptosomal membranes or the uptake and release of GABA in synaptosomes. Glutamate (3.75 or 7.5mmol intraventricularly) increased the level of cyclic GMP in the cerebellum, but IPTBO did not alter the cerebellar glutamate level. Results suggest that the elevation of cerebellar cyclic GMP caused by the bicyclic phosphates is not due to activation of the climbing fibers but to a GABA antagonistic effect; the mechanism of action of the bicyclic phosphates may be similar to that of picrotoxin. 37 references. (Author abstract modified)

001407 McCaleb, M. L.; Myers, R. D. Dept. of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Striatal dopamine release is altered by glucose and insulin during push-pull perfusion of the rat's caudate nucleus.** Brain Research Bulletin. 4(5):651-656, 1979.

In a study of the sensitivity of catecholaminergic neurons to glucose and insulin, a single site in the caudate/putamen of unrestrained, fasted Long-Evans or Sprague-Dawley male rats was labeled with tritiated dopamine (3H-DA) or norepinephrine (3H-NE) and then perfused with artificial CSF. At the midpoint of a sequence of seven push/pull perfusions, the rat was given food pellets or D-glucose (55mcg/mcl), insulin (4mU/mcl), or 2-deoxy-D-glucose (2-DG, 10mcg/mcl) was added to the CSF perfusate. The efflux of 3H-DA increased when rats ate the pellet and during subsequent perfusions. An immediate rise in 3H-DA efflux was also seen when insulin was added to the perfusate, but 2-DG had no effect. A slight suppression in efflux was seen during perfusion of D-glucose, but a consistent elevation of radioactivity was observed after the perfusion. The patterns of 3H-NE release were similar to those of 3H-DA, but the magnitude of the change was smaller. Results suggest that striatal DA may have a functional role in the regulation of food intake. 30 references. (Author abstract modified)

001408 McCall, Robert B.; Aghajanian, George K. Cardiovascular Diseases Research Unit, Upjohn Company, Kalamazoo, MI 49001 **Hallucinogens potentiate responses to serotonin and norepinephrine in the facial motor nucleus.** Life Sciences. 26(14):1149-1156, 1980.

The effect of hallucinogens on the facilitating action of serotonin (5-HT) and norepinephrine (NE) in the facial nucleus was examined with 45 male Charles River rats. Intravenous administration of d-lysergic acid diethylamide (LSD), mescaline, or psilocin had no effect by themselves on the glutamate-induced excitation of facial motoneurons. In contrast, the facilitation of facial neuron excitation by iontophoretically applied 5-HT and NE was enhanced six to ten fold by these hallucinogens. Iontophoretic application of LSD or mescaline also markedly potentiated the facilitating effect of 5-HT and NE. The nonhallucinogenic ergot derivatives lisuride and methysergide failed to potentiate the facilitating effects of 5-HT or NE. It is suggested that hallucinogens potentiate the effect of monoamines on facial motoneurons by increasing the sensitivity of 5-HT and NE receptors. 24 references. (Author abstract modified)

001409 McCulloch, James; Savaki, Helen E.; McCulloch, Mailis C.; Sokoloff, Louis. University of Glasgow, Glasgow G12 8QQ, Scotland **Retina-dependent activation by apomorphine of metabolic activity in the superficial layer of the superior colliculus.** *Science*. 207(4428):313-315, 1980.

The effects of the dopamine agonist apomorphine on local cerebral glucose utilization in the rat was examined by means of the carbon 14 labeled deoxyglucose method. The studies demonstrated a dose dependent metabolic activation in the superficial layer of the superior colliculus in the rat. Apomorphine stimulated glucose utilization in a number of other cerebral structures, but only the effect in the superficial layer of the superior colliculus depended on an intact retinal input. This effect was present with the animal in the light or in the dark, but was abolished by enucleation, which left the effects in other cerebral structures unimpaired. Activation of the superficial layer of the superior colliculus appeared to be secondary to an action of apomorphine on dopaminergic systems within the retina. 13 references. (Author abstract modified)

001410 McGinnis, Marilyn Y.; Gordon, John H.; Gorski, Roger A. Gorski: Dept. of Anatomy, UCLA School of Medicine, Los Angeles, CA 90024 **Time course and localization of the effects of estrogen on glutamic acid decarboxylase activity.** *Journal of Neurochemistry*. 34(4):785-792, 1980.

Two approaches were used in an attempt to characterize the effect of estrogen on glutamic acid decarboxylase (GAD) activity in ovariectomized rats. When estradiol-17 β (E2) was unilaterally implanted in one of five different brain areas, estrogen implanted in the preoptic area and the ventromedial nucleus was ineffective; however, GAD activity was decreased in the substantia nigra (SN) when E2 was implanted into the caudate nucleus or amygdala and in the ventral tegmental region (VTR) when implanted into the nucleus accumbens septi. When the time course of changes in GAD activity was measured in ovariectomized rats given a single systemic injection of either 8 mcg estradiol benzoate (EB) or oil, GAD activity in the SN was maximally suppressed 29 hours after EB, whereas decreased GAD activity in the VTR was apparent 12 hours after EB but had returned to normal by 29 hours. Results suggest that there may be two separate and distinct gamma-aminobutyric acid pathways which are differentially responsive to estrogen. 37 references. (Author abstract modified)

001411 McKenna, Mary L.; Ho, B. T. Texas Research Institute of Mental Sciences, Houston, TX 77030 **The role of dopamine in the discriminative stimulus properties of cocaine.** *Neuropharmacology*. 19(3):297-303, 1980.

The discriminative stimulus properties of cocaine were studied in male Sprague-Dawley rats, and Ss discriminating 10mg/kg cocaine from saline were tested with several agonists. Meth-

ylphenidate, d-amphetamine, and apomorphine generalized to cocaine. Catapresan, imipramine, fenfluramine, pseudococaine, cocaine methiodide, strychnine, procaine, and mescaline did not generalize. The receptor antagonist haloperidol shifted the cocaine dose response curve to the right and diminished the maximum response. Cinaserin, atropine, phenoxybenzamine, and sotolol had no effect. The catecholamine depletor, reserpine shifted the dose response curve to the right and diminished the maximum response. Alpha-methyl-para-tyrosine had no effect. The results suggest that the discriminative stimulus properties of cocaine are mediated by the release of dopamine from the CNS. 38 references. (Author abstract modified)

001412 McLennan, I. S.; Lees, G. J. Dept. of Pharmacology, John Curtin School of Medical Research, Canberra City, A.C.T., Australia **The development of tryptophan hydroxylase in the chicken brain: effects of p-chloroamphetamine and antagonists of serotonin, noradrenaline and dopamine.** *Neuropharmacology*. 18(3):269-277, 1979.

The development of tryptophan hydroxylase in the midbrain and hindbrain of the chicken was examined. In general, specific activities were low prior to day 14 of egg incubation and reached a plateau around hatching (day 21). The total amount of tryptophan hydroxylase continued to increase after hatching in the hindbrain but not in the midbrain. Injection of the dopamine antagonists haloperidol, (-)-butaclamol, fluphenazine, and methiothepin into the air sac of chicken eggs incubated for 14 days resulted in elevated levels of tryptophan hydroxylase in the hindbrain-I region of 7-day-old chickens. Injections of haloperidol into 7-day-old chickens had no effect on tryptophan hydroxylase levels at 21 days of age. Treatment of eggs with apomorphine, piribedil, methysergide, cyproheptadine, p-chloroamphetamine, or propranolol had no significant effect on any brain region examined. 43 references. (Author abstract modified)

001413 McRae-Degueurce, Amanda; Pujol, Jean-Francois. Dept. de Neurochimie Fonctionnelle, INSERM U 171, Université Claude Bernard, 8, Avenue Rockefeller, F-69373 Lyon, France **Correlation between the increase in tyrosine hydroxylase activity and the decrease in serotonin content in the rat locus coeruleus after 5,6-dihydroxytryptamine.** *European Journal of Pharmacology*. 59(1/2):131-135, 1979.

Endogenous 5-hydroxytryptamine (5-HT) content and tyrosine hydroxylase (TH) activity were determined in the locus coeruleus (LC) of male OFA rats treated with 5,6-dihydroxytryptamine (5,6-HT) alone or in combination with the 5-HT uptake inhibitors fluoxetine and citalopram. Results revealed a correlation between the increase in TH activity and the decrease in 5-HT concentration in the LC. Citalopram was more effective than fluoxetine in protecting 5-HT neurons from the neurotoxic effects of 5,6-HT. It is suggested that noradrenaline metabolism in the LC is governed by 5 serotonergic raphe neurons. 11 references. (Author abstract modified)

001414 Means, Jeffrey R.; Schnell, R. Craig. Dept. of Pharmacology and Toxicology, School of Pharmacy and Pharmaceutical Sciences, Purdue University, West Lafayette, IN 47907 **Interaction between cadmium and phenobarbital on the activity of the hepatic microsomal monooxygenase system in the male rat.** *Research Communications in Chemical Pathology and Pharmacology*. 27(1):187-190, 1980.

The effects of cadmium and phenobarbital on the hypnotic response and hepatic microsomal biotransformation of hexobarbital were studied in male Sprague-Dawley rats. Cadmium significantly potentiated the duration of hypnosis and decreased the rate of drug biotransformation. Phenobarbital significantly reduced the duration of hypnosis and stimulated the rate of bio-

transformation. When both agents were administered concomitantly, their effects cancelled each other. 11 references. (Author abstract modified)

001415 Meibach, Richard C.; Glick, Stanley D.; Cox, Russel; Maayani, Saul. Department of Pharmacology, Mount Sinai School of Medicine, New York, NY 10029 **Localisation of phenacyclidine-induced changes in brain energy metabolism.** *Nature*. 282(5739):625-626, 1979.

Using a recently developed procedure of directly monitoring 2-deoxy-D-glucose consumption before and after phenacyclidine (PCP) injection, autoradiographic evidence of changes in neuronal activity in cerebral glucose activity was examined. Female Sprague-Dawley rats were employed. A striking effect of PCP on local cerebral glucose metabolism is reported with major sites of increased metabolism being components of the limbic lobe. Results are discussed in terms of the emotional disorders caused by PCP and their relation to the limbic system. 8 references. (Author abstract modified)

001416 Melamed, Eldad; Hefti, Franz; Liebman, James; Schlosberg, Arthur J.; Wurtman, Richard J. Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Sciences, MIT, Cambridge, MA 02139 **Serotonergic neurones are not involved in action of L-dopa in Parkinson's disease.** *Nature*. 283(5749):772-774, 1980.

Decarboxylation of exogenous dopa was examined in an animal model of parkinsonism (rats with nigrostriatal lesions which were further subjected to lesions of the striatal serotonergic projections). Data indicate that combined destruction of striatal dopaminergic and serotonergic terminals had little additional effect, beyond destroying dopaminergic neurones, on dopa's ability to enhance striatal dopamine release. Findings, therefore, do not favor the concept that serotonergic neurones are involved in mediating the therapeutic effect of L-dopa in the treatment of Parkinson's disease. 40 references. (Author abstract modified)

001417 Melamed, Eldad; Hefti, Franz; Wurtman, Richard J. Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Diminished decarboxylation of L-dopa in rat striatum after intrastriatal injections of kainic acid.** *Neuropharmacology*. 19(4):409-411, 1980.

The effects of intrastriatal injections of kainic acid on decarboxylation of L-dopa and dopamine (DA) activity in rat striatum following dopa administration were investigated. Injection of kainic acid into rat striatum reduced striatal dopa decarboxylase activity by 20% as compared with that in control unlesioned sides. After administration of L-dopa, concentrations of DA (but not dopa) were lower (by 33%) in lesioned than in control striata indicating decreased *in vivo* formation of DA from exogenous dopa after kainate lesions. These findings suggest that in the rat, a significant part of striatal dopa decarboxylase activity is localized in neurons originating within the striatum (interneurons and/or efferents) whose perikarya are selectively destroyed by kainic acid. 12 references. (Author abstract modified)

001418 Meller, E.; Friedhoff, A. J.; Friedman, E. Neuropsychopharmacology Research Unit, New York University School of Medicine, New York, NY 10016 **Differential effects of acute and chronic haloperidol treatment on striatal and nigral 3,4-dihydroxyphenylacetic acid (DOPAC) levels.** *Life Sciences*. 26(7):541-547, 1980.

The differential effects of acute and chronic haloperidol treatment on striatal and nigral 3,4-dihydroxyphenylacetic acid

(DOPAC) levels were investigated. Chronic haloperidol treatment of rats (4 weeks, 0.5 or 1mg/kg) resulted in a significant attenuation of the large DOPAC rise seen in the corpus striatum after acute treatment. This tolerance effect was observed both shortly following termination of chronic treatment and on challenge with a low dose (0.1mg/kg) of the drug 6 to 8 days later. In contrast, acute haloperidol treatment resulted in only a small and nonsignificant elevation of DOPAC levels in the substantia nigra, while chronic treatment caused a larger and significant increase in levels of the metabolite. Moreover, the latter effect was also observed in response to haloperidol challenge 6 to 8 days after discontinuation of drug treatment. The differential pattern of response in these two brain regions is discussed in relation to possible mechanisms mediating striatal tolerance and to recent observations regarding changes in nigral dopamine cell firing after chronic haloperidol treatment. 25 references. (Author abstract modified)

001419 Meltzer, H. Y.; So, Rebecca. Department of Psychiatry, University of Chicago Pritzker School of Medicine, Chicago, IL 60637 **Effect of morphine, beta-endorphin and leu-enkephalin on 3H-spiroperidol binding to bovine pituitary membranes.** *Life Sciences*. 25(6):531-535, 1979.

The ability of morphine, leu-enkephalin and beta-endorphin to antagonize the binding of 3H-spiroperidol to bovine anterior pituitary membranes was studied. All three drugs were virtually inactive despite their ability to stimulate prolactin secretion *in vivo* and the reported ability of morphine to antagonize the inhibitory effect of dopamine on prolactin release from rat hemipituitaries. These results suggest that opiates do not produce their direct effect on prolactin secretion at the pituitary level through an effect on the 3H-spiroperidol binding site. The opiates may antagonize the effect of dopamine at a component of the dopamine receptor which is independent of the 3H-spiroperidol binding site, or the opiates may stimulate prolactin secretion by an effect on the lactotrophs which is independent of dopamine. 26 references. (Author abstract)

001420 Menon, M. K.; Tseng, Liang-Fu; Loh, H. H.; Clark, W. G. Psychopharmacology Research Laboratory, VA Medical Center, Sepulveda, CA 91343 **An electromyographic method for the quantitative evaluation of narcotic analgesics in rats.** *Neuropharmacology*. 19(3):231-236, 1980.

A new EMG method was developed for the quantitative evaluation of narcotic analgesics in rats anesthetized with urethane. D-amphetamine increased the amplitude and frequency of myoclonic twitch activities (MTA) of suprahyoid muscle. Morphine and several other narcotic analgesics antagonized the amphetamine-induced MTA and their relative inhibitory potency closely paralleled analgesic potencies. Etorphine was 2,000 to 3,500 times more potent than morphine, while meperidine showed only 2% of its activity. Levorphanol was 3 to 4 times more potent than morphine, while dextrophan was inactive. L-methadone was 10 times as potent as d-methadone. The inhibition of MTA by morphine was completely reversed by naloxone, while its inhibition by haloperidol or pentobarbitone was not influenced. The measurement of the EMG of suprahyoid muscle in rats provides a convenient test and reliable means of assessing the central effect of narcotic analgesics. 26 references. (Author abstract modified)

001421 Mesher, Richard A.; Schwartzkroin, Philip A. 183(2):472-476, 1980. Seattle, WA 98195 **Can CA3 epileptiform discharge induce bursting in normal CA1 hippocampal neurons?** *Brain Research*. Schwartzkroin: Dept. of Neurological Surgery, University of Washington.

Two hypotheses concerning the generation of intracellular depolarization shifts (DSs) which are reflected in extracellular spike field potentials in acute cortical or hippocampal foci were evaluated. One hypothesis contends that increased excitatory input, resulting in giant excitatory postsynaptic potentials (EPSPs), generates the DS; the other hypothesis, based on recent work using the *in vitro* hippocampal slice preparation, suggests that intrinsic neuronal properties could account for DS generation. Penicillin was applied focally to the CA3 region *in vitro* and the effects of CA3 epileptiform input to CA1 neurons were observed. Results do not support the notion that the epileptiform DS is the result of enhanced excitatory input. Unlike experiments in which CA1 neurons were directly exposed to penicillin as well as to synchronous (A3) drive, the present paradigm allowed CA1 cells exposure only to the CA3 input. The absence of DS activity in CA1 neurons under such conditions suggests that penicillin must exert effects on local cellular membranes and/or circuitry before signs of epileptogenesis appear. Results are consistent with the view that penicillin-induced epileptiform activity may be triggered by excitatory input, but that the DS itself is attributable to a release of intrinsic cellular properties. 20 references.

001422 Messing, Rita B.; Dodge, Clara; Waymire, Jack C.; Lynch, Gary S.; Deadwyler, Sam A. Dept. of Psychobiology, University of California, Irvine, CA 92717 **Morphine induced increases in the incorporation of 3H-thymidine into brain striatal DNA.** *Brain Research Bulletin*. 4(5):615-619, 1979.

The uptake of tritiated thymidine into DNA fractions of male Sprague-Dawley rat brain regions was measured following *in vivo* administration of (methyl-3H)-thymidine and morphine. Acute morphine administration (10mg/kg, 30 minutes prior to 3-H-thymidine) increased the incorporation of 3H-thymidine into DNA in striatum, and this effect was antagonized by pretreatment with 1mg/kg naloxone. An autoradiographic study showed that the 3-H-thymidine was localized in nuclei in cells of the subependymal layer lining the lateral ventricles, an area of glial cell proliferation of adult rats. No change in 3-H-thymidine incorporation into DNA was observed in any area of the brain in morphine addicted rats or in rats undergoing naloxone precipitated withdrawal. Results suggest that opiates may induce permanent anatomical changes in the brain, including alteration in neuroglial interactions. 27 references. (Author abstract modified)

001423 Meyerson, Laurence R.; Cashaw, Jesse L.; McMurtrey, Kenneth D.; Davis, Virginia E. Dept. of Biochemistry, Hoechst-Roussel Pharmaceuticals, Inc., Route 202-206 North, Somerville, NJ 08876 **Stereoselective enzymatic O-methylation of tetrahydropapaveroline and tetrahydroxyberberine alkaloids.** *Biochemical Pharmacology*. 28(11):1745-1752, 1979.

The enzymatic O-methylation patterns of the racemates and optical isomers of tetrahydropapaveroline (THP) and 2,3,10,11-tetrahydroxyberberine (THB) by a rat liver catechol-O-methyltransferase preparation were studied. Reaction products were separated and isolated by high pressure liquid chromatography, and structural identity was confirmed by synthesis and gas chromatography/mass spectrometry. The positions of enzymatic O-methylations were markedly influenced by the particular optical isomeric form of substrate employed. The optical isomers and racemates of THP and THB were mainly mono-O-methylated with trace amounts of di-O-methylation. The mono-O-methylations of THP were contained exclusively in the isoquinoline ring at positions 6 or 7, while mono-O-methylations of THB occurred at the vicinal hydroxyl groups of both rings A and D. Results suggested that vicinal hydroxyl moieties of THP and THB are mono-O-methylated at either of the sites and that the magnitude of the positional isomer product ratio reflects the op-

tical isomeric orientation in which the substrate binds to the enzyme. 29 references. (Author abstract modified)

001424 Miksic, Stephen Leslie. University of Rhode Island **Evaluation of pain as a discriminative stimulus in the rat.** *Dissertation Abstracts International*. 39(7):3577-B, 1979. Ann Arbor, Univ. Microfilms No. 7821167, 113p., 1978.

The effects of intraperitoneal injections of phenyl-p-benzoquinone (PBQ) were examined in three experiments with hooded rats to evaluate its action as a potential model for the study of produced dose dependent writhing which could be blocked by morphine. In a performance task, PBQ was found to be a discriminative stimulus because of its irritant quality. It is concluded that the problems of toxicity and performance reliability must be overcome before PBQ can be used as a practical screening procedure for evaluation analgesic drug effects. (Journal abstract modified)

001425 Miller, Harold Hampton, Jr. University of Texas Health Science Center at Dallas **Comparison of amphetamine and non-amphetamine stimulants on dopamine metabolism in corpus striatum of the rat.** (Ph.D. dissertation). *Dissertation Abstracts International*. 39(8):3791-B, 1979. Ann Arbor, Univ. Microfilms No. 7902467, 93p., 1978.

The effects of amfonelic acid and amphetamine on dopamine metabolism was examined in corpus striatum of the rat. Amfonelic acid altered metabolism of new dopamine similarly to that of preformed dopamine, raising labelled metabolite levels while lowering 3H-dopamine content despite an enhancement of dopamine synthesis. The action of d-amphetamine on metabolism of new dopamine was the opposite of amfonelic acid. Thus, d-amphetamine combined with haloperidol raised 3H-dopamine even in rats treated with monoamine oxidase inhibitor (pargyline). Similar actions of d-amphetamine were seen on total dopamine. Thus, d-amphetamine raised total dopamine with or without haloperidol even in the presence of pargyline, and also slowed the dopamine decline seen after haloperidol and alpha-methyltyrosine. It is suggested that amphetamine may release newly synthesized dopamine from a special site, with some reaching the synaptic cleft and a second portion accumulating in the dopamine storage system; while amfonelic acid appears to facilitate impulse induced dopamine overflow. (Journal abstract modified)

001426 Minchin, Rodney F.; Ilett, Kenneth F.; Madsen, Barry W. Ilett: Dept. of Pharmacology, University of Western Australia, Nedlands, Western Australia, 6009, Australia **Chlorphentermine binding in rat lung subcellular fractions and its displacement by desmethylimipramine.** *Biochemical Pharmacology*. 28(15):2273-2278, 1979.

The effect of desmethylimipramine (DMI) on chlorphentermine (CP) binding in male Wistar rat lung subcellular fractions was studied. CP binding was greater in the microsomal and 15,000g fractions than in cytosol. With all isotherms, CP binding consisted of a specific, saturable component and a nonspecific partitioning component. In general, CP binding decreased as DMI concentration increased, but this relationship was not consistent with direct competitive binding. Results suggest that DMI and CP interact in the lung via a cooperative mechanism involving binding-induced conformational transitions. The possible role of phospholipids in the binding of basic amines in lung is discussed. 22 references. (Author abstract modified)

001427 Minegishi, A.; Fukumori, R.; Satoh, T.; Kitagawa, H.; Yanaura, S. Satoh: Dept. of Biochemical Pharmacology, Faculty of Pharmaceutical Sciences, Chiba University, Yayoi-cho 1-33, Japan **Changes in serotonin turnover and the brain sensitivity to barbiturates by disulfiram treatment in rats.** *Research Commu-*

nications in *Chemical Pathology and Pharmacology*. 24(2):273-287, 1979.

The effects of disulfiram and barbiturates on serotonin (5-HT) turnover and the effect of disulfiram on brain sensitivity to barbiturates were examined in male Wistar rats. Treatment with 200mg/kg i.p. disulfiram prolonged the duration of barbiturate-induced hypnosis, indicating increased brain sensitivity to barbiturates. Disulfiram also reduced the turnover and level of 5-HT, but this effect was less potent than that exerted by 80mg/kg i.p. sodium phenobarbital. Simultaneous administration of disulfiram and phenobarbital resulted in severe retardation of 5-HT metabolism. Results suggest that disulfiram potentiates the hypnotic action of barbiturates by altering 5-HT metabolism in rat brain. 27 references. (Author abstract modified)

001428 Mitchell, P. R.; Martin, I. L. MRC Neuropharmacology Unit, Medical School, Birmingham, England **Facilitation of striatal potassium-induced dopamine release - novel structural requirements for a presynaptic action of benzodiazepines**. *Neuropharmacology*. 19(1):147-150, 1980.

A series of benzodiazepines was tested for ability to facilitate the potassium-induced release of tritiated dopamine from rat striatal tissue. Results indicate that benzodiazepines have a presynaptic action mediated by a novel benzodiazepine recognition site with distinct structural requirements. The presynaptic activity of the benzodiazepines does not correlate with their potencies in binding experiments or in empirical pharmacological tests. Of the drugs tested, medazepam appeared to have the most selectively presynaptic action. 6 references. (Author abstract modified)

001429 Mitra, Chhanda; Guha, S. R. Indian Institute of Experimental Medicine, Calcutta 32, India **Inhibition patterns of monoamine oxidase in sub-fractions of rat brain mitochondria in presence of some selective inhibitors**. *Biochemical Pharmacology*. 28(7):1135-1137, 1979.

The inhibition of monoamine oxidase (MAO) activity in different mitochondrial subfractions of rat brain was studied in the presence of harmine, harmaline, and deprenyl. Tyramine and serotonin were used as substrates. Results showed that type-A and type-B MAO are distributed in different ratios among the mitochondrial subfractions. 18 references. (Author abstract modified)

001430 Miyauchi, Tatsuo; Oikawa, Sumiko; Kitada, Yoshimi. Dept. of Pharmacology, Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan **Effects of lithium chloride on the cholinergic system in different brain regions in mice**. *Biochemical Pharmacology*. 29(4):654-657, 1980.

The effects of a single dose and of chronic administration of lithium chloride (LiCl) on steady state levels of acetylcholine (ACh) and choline (Ch) and on ACh turnover by an indirect method using hemicholinium-3 (HC-3), in different brain regions in mice were investigated. When the levels of ACh and Ch in the mouse brain regions, which were obtained using a near freezing method for sacrifice, were compared with those obtained by a microwave irradiation method, the values for ACh were identical to those in the same strain of mice after 1.3kW microwave radiation for 2 seconds, although Ch level showed higher values than those reported by Nordberg (1977). Results indicate that a single administration of a high dose of LiCl has no measurable effect on the steady state level and the HC-3-induced depletion of ACh in the five brain regions tested, and that chronic lithium administration reduces the activity of cholinergic neurons in cortex and increases both the ACh level and the rate of HC-3-induced depletion of ACh in midbrain tissue at

a plasma concentration of Li within the therapeutic range. 16 references

001431 Mobley, Philip L.; Sulser, Fridolin. Vanderbilt University School of Medicine, Nashville, TN 37217 **Norepinephrine stimulated cyclic AMP accumulation in rat limbic forebrain slices: partial mediation by a subpopulation of receptors with neither alpha nor beta characteristics**. *European Journal of Pharmacology*. 60(2/3):221-227, 1979.

Isoproterenol and norepinephrine (NE) both increased cyclic AMP in slices of male Sprague-Dawley rat limbic forebrain, and these responses were enhanced in the presence of the phosphodiesterase inhibitor RO20-1724. No accumulation of cyclic AMP was observed after the addition of dopamine, serotonin, methoxamine, or phenylephrine, even in the presence of RO20-1724; this suggests that these agents do not activate adenylate cyclase or that their receptors are not coupled to adenylate cyclase. The beta-agonist isoproterenol has high affinity for this adenylate cyclase system, but showed only 20 to 30% of the maximal activity of NE. Isoproterenol did not interfere with the agonist activity of NE, and the effects of NE and isoproterenol were not additive. Results suggest that two populations of NE receptors coupled to adenylate cyclase are present in the limbic forebrain, one with beta characteristics and the other with neither alpha nor beta characteristics. 26 references. (Author abstract modified)

001432 Mohrland, J. Scott; Craigmill, A. L. Dept. of Pharmacology, University of Iowa College of Medicine, Iowa City, IA 52242 **Effect of lethal doses of morphine on brain amines in isolated and aggregated mice**. *Pharmacology Biochemistry and Behavior*. 12(2):313-315, 1980.

Brain levels of norepinephrine, dopamine and serotonin were measured in isolated and aggregated mice after lethal doses of morphine. Although morphine significantly lowered all three brain monoamines there were no significant differences between isolated and aggregated mice. Measurements of brain morphine concentrations also failed to demonstrate any differences which could account for the difference in lethality observed in isolated and aggregated mice. These results further differentiate the aggregation effect of morphine toxicity from that of amphetamine toxicity. 21 references. (Author abstract modified)

001433 Morichi, Riccardo; Pepeu, Giancarlo. Dept. of Pharmacology, University of Florence, Viale Morgagni 65, I-50134 Florence, Italy **A study of the influence of hydroxyzine and diazepam on morphine antinociception in the rat**. *Pain*. 7(2):173-180, 1979.

The influence of hydroxyzine, a minor tranquilizer devoid of hypnotic activity, on the action of morphine on nociception and locomotor activity was investigated in the rat and was compared with diazepam. Electrical tail stimulation data showed that the drug had little direct analgesic activity but markedly potentiated the morphine effects on the vocalization after-discharge, which represents the affective component of pain. Equimolar doses of diazepam showed antinociceptive properties which were not blocked by naloxone and also potentiated morphine action on the affective pain component. Hydroxyzine alone had no effect in the tail flick test; hydroxyzine potentiated morphine at the largest the largest dose tested but the antinociception at lower doses. Diazepam alone had little effect but potentiated morphine antinociception only at the largest dose. Both hydroxyzine and diazepam potentiated morphine depression of locomotor activity but diazepam was significantly more active. 13 references. (Author abstract modified)

001434 Morin, Ann M.; Wasterlain, Claude G. Neurology and Epilepsy Research Laboratories, VA Medical Center, Sepul-

veda, CA The binding of 3H-isoguvacine to mouse brain synaptic membranes. *Life Sciences*. 26(15):1239-1245, 1980.

3H-Isoguvacine (3H-IGV) binding to mouse synaptic membranes was studied. 3H-IGV was shown to bind to a mouse forebrain synaptic membrane preparation; the specific binding was displaceable by GABA, muscimol, and bicuculline, but not by picrotoxin or diaminobutyric acid. Kinetic data suggest two binding affinities. Highest levels of binding were observed in the cerebellum, cortex, and hippocampus. It is suggested that isoguvacine binds to GABA binding sites and therefore represents a new ligand for measuring GABA receptor binding. 16 references. (Author abstract modified)

001435 Mucha, R. F.; Kalant, H. Addiction Research Foundation of Ontario, 33 Russell Street, Toronto, Ontario, Canada M5S 2S1 Failure of prolyl-leucyl-glycinamide to alter analgesia measured by the Takemori test in morphine-pretreated rats. *Journal of Pharmacy and Pharmacology*. 31(8):572-573, 1979.

The effects of prolyl-leucyl-glycinamide (PLG) on analgesia was examined in 141 male Wistar rats, pretreated with morphine. Several morphine test doses, two PLG treatment doses, and two tests of analgesia were used. Separate analyses of variance indicated highly significant overall effects of morphine for hotplate and tailflick tests. However, there were no appreciable effects of PLG; neither overall PLG nor PLG by morphine interactions were significant. Results are discussed in terms of previous research, particularly that of van Ree and de Wied (1976). 14 references.

001436 Murrin, L. Charles; Gale, Karen; Kuhar, Michael J. Kuhar: Dept. of Pharmacology, Johns Hopkins University School of Medicine, 725 North Wolfe St., Baltimore, MD 21205. Autoradiographic localization of neuroleptic and dopamine receptors in the caudate-putamen and substantia nigra: effects of lesions. *European Journal of Pharmacology*. 60(2/3):229-235, 1979.

The localization of neuroleptic receptors was studied in the caudate-putamen (CP) and the zona compacta of the substantia nigra of male Sprague-Dawley rats, using light microscopic autoradiography of 3H-spiroperone binding sites. Lesion of the dopaminergic input to the CP produced an increase in receptors in the CP, possibly reflecting denervation supersensitivity. Kainic acid lesions and decortication produced decreases of 61% and 18% in striatal receptors. Lesion of the nigrostriatal dopaminergic pathway produced a 48% decrease in receptor sites in the substantia nigra zona compacta, but intrastriatal kainic acid and striatonigral pathway lesions had no significant effect. Results suggest that most dopamine (DA) receptors in the CP are on intrastriatal neurons, but some are localized to afferents from the cortex. The majority of DA receptors in the zona compacta that bind neuroleptics are located on cell bodies and processes of dopaminergic neurons and are anatomically distinct from DA stimulated adenylate cyclase sites. 46 references. (Author abstract modified)

001437 Murrin, L. Charles; Kuhar, Michael J. Kuhar: Dept. of Pharmacology, Johns Hopkins University School of Medicine, 725 North Wolfe St., Baltimore, MD 21205 Dopamine receptors in the rat frontal cortex: an autoradiographic study. *Brain Research*. 177(2):279-285, 1979.

Dopamine receptors were localized in the frontal cortex at the light microscopic level by autoradiographic methods in male Sprague-Dawley rats. The animals were pretreated with pipamperone, a drug with serotonergic properties, to reduce the serotonergic component of (3H)spiroperone binding. At the level of forceps minor, high densities of dopamine receptors were found in the deeper layers of the cingulate cortex, in the region above

the rhinal sulcus, and in an area dorsal to the accumbens. 30 references. (Author abstract modified)

001438 Nadler, J. Victor; Shelton, David L.; Perry, Bruce W.; Cotman, Carl W. Dept. of Pharmacology, Duke University Medical Center, Durham, NC 27710 Regional distribution of (3H)kainic acid after intraventricular injection. *Life Sciences*. 26(2):133-138, 1980.

The regional distribution of (3H)kainic acid was studied after intraventricular injection of a dose that selectively destroys the pyramidal cells of rat hippocampal area CA3. Only about one third of the injected radioactivity was recovered in the brain 15 min later, but the residual radioactivity disappeared at a much slower rate. (3H)kainic acid distributed rather evenly throughout the brain; there was no correlation between accumulation of radioactivity and neurotoxicity. Almost 90% of the radioactivity in sucrose homogenates was recovered in the high speed supernatant. No cerebral metabolism of (3H)kainic acid was detected by thin layer chromatography. These data rule out the possibility that a lethal accumulation of the toxin by hippocampus accounts for the preferential vulnerability of hippocampal pyramidal cells. 22 references. (Author abstract modified)

001439 Nahorski, Stefan R.; Howlett, David R.; Redgrave, Peter. Dept. of Pharmacology and Therapeutics, Medical Sciences Building, University of Leicester, University Road, Leicester, LE1 7RH, England Loss of beta-adrenoceptor binding sites in rat striatum following kainic acid lesions. *European Journal of Pharmacology*. 60(2/3):249-252, 1979.

Intrastriatal injection of kainic acid (5nM) to female hooded Lister rats led to a severe destruction of nerve cell bodies throughout the caudate-putamen complex and an extensive proliferation of glial cells. Lesioned striata displayed a 23% loss of beta-adrenoceptor binding sites 21 to 24 days after injection of kainic acid, and this loss of sites was selective for the beta-receptor population. These findings do not rule out a partial glial localization for beta-adrenoceptors, but they do indicate that some beta-receptors are present on striatal perikarya. 12 references. (Author abstract modified)

001440 Nakadate, Teruo; Muraki, Takamura; Tokunaga, Yukiko; Kato, Ryuichi. Dept. of Pharmacology, School of Medicine, Keio University, Shinanomachi, Shinjuku-ku, Tokyo 160, Japan Effect of chlorpromazine on plasma adenosine 3',5'-cyclic phosphate level. *Biochemical Pharmacology*. 29(5):801-805, 1980.

The increase in the plasma cyclic 3',5'-adenosine phosphate (cAMP) level in male mice following subcutaneous injection of chlorpromazine hydrochloride (CPZ) at a dose of 10mg/kg was investigated. Propranolol and hexamethonium abolished the elevation of plasma cAMP induced by CPZ. Phenolamine could not inhibit the effect of CPZ. Adrenalectomy completely inhibited the elevation of plasma cAMP produced by CPZ. Intracerebroventricular administration of CPZ also increased plasma cAMP levels. These findings indicate that CPZ activated the sympathetic nervous system by acting on the CNS, thereby increasing plasma cAMP levels through the stimulation of beta-adrenoceptors mainly by catecholamines released from the adrenal medulla. 16 references. (Author abstract)

001441 Narasimhachari, N.; Callison, D.; Lin, R.-L. Dept. of Psychiatry, Medical College of Virginia, Richmond, VA 23298 Effect of MAO inhibitors on the tissue distribution of dimethyltryptamine, 5-methoxydimethyltryptamine and bufotenin after their intraperitoneal administration in rat. *Research Communications in Psychology, Psychiatry and Behavior*. 4(3):257-268, 1979.

The effect of MAO inhibitors upon tissue distribution of dimethyltryptamine (DMT), bufotenin and 5-methoxydimethyltryptamine (5-MeODMT) injected intraperitoneally was investigated in rats. One group of rats received 5mg/kg and a second group 10mg/kg of each of the compounds. Other groups of rats were pretreated with 1mg of tranylcypromine, an MAO inhibitor, injected 1 hour before experimental compounds were administered. Results indicated that the compounds were found at higher levels and for a longer period, in animals pretreated with tranylcypromine. DMT and 5-MeODMT were identified in the liver, lung, kidney and heart at intervals varying from 15 minutes to 2 hours but were not found in the bloodstream after 30 minutes. Bufotenin did not pass the blood-brain barrier in rats not pretreated with tranylcypromine, but it was found in the lungs and liver as a conjugate (glucuronide). In the rats pretreated with tranylcypromine, phenelzine or pargyline, bufotenin was found to pass the blood-brain barrier. It is concluded that MAO inhibitors are acting by a mechanism other than MAO inhibition in producing changes in the permeability of the blood-brain barrier in rats. 19 references. (Author abstract modified)

001442 Natsuki, R.; Hitzemann, R. J.; Loh, H. H. Langley Porter Neuropsychiatric Institute, San Francisco, CA 94143 **Influence of morphine, beta-endorphin and naloxone on the synthesis of phosphoinositides in the rat midbrain.** *Research Communications in Chemical Pathology and Pharmacology*. 24(2):233-250, 1979.

The effects of morphine, beta-endorphin, and naloxone on the initial incorporation of 32Pi and (3H)glycerol into 1-phosphatidylinositol-3,4-bisphosphate (TPI), 1-phosphatidylinositol-4-phosphate (DPI), and phosphatidylinositol (PI) were measured in discrete subcellular fractions of the male Sprague-Dawley rat midbrain. Morphine and beta-endorphin significantly increased microsomal 32Pi incorporation into TPI and PI, but not DPI. Neither morphine nor beta-endorphin significantly altered levels of (3H)TPI or (3H)DPI, but both agents significantly increased (3H)PI levels. The effects of morphine were blocked by naloxone and decreased after chronic morphine treatment. However, naloxone treatment alone mimicked all the effects of morphine except the increased incorporation of (3H)glycerol into PI. Chronic morphine treatment significantly increased the incorporation of 32Pi into synaptic TPI and DPI in cortical and subcortical synaptic membranes. Results suggest that mechanisms of opioid action are closely associated with changes in the turnover of brain phosphoinositides. 31 references. (Author abstract modified)

001443 Nau, Heinz; Liddiard, Colin. Institut für Toxikologie und Embryopharmakologie, Garystrasse 9, D-1000 Berlin 33, Germany **Postnatal development of sex-dependent differences in the metabolism of diazepam by rat liver.** *Biochemical Pharmacology*. 29(3):447-449, 1980.

The metabolism of diazepam by the 6,000g supernatant of rat liver homogenate obtained from male and female rats at different ages was studied in the Wistar and BD rat strains. Results indicated that the rate of 3-hydroxylation of diazepam by the adult male rat exceeds that of the adult female rat by a factor of 10 (BD strain) or 5.2 (Wistar strain). The rate of N-methylation showed much smaller differences. For the neonatal rat, neither 3-hydroxylating nor N-demethylating activities showed a sex dependent difference. Evidence also indicated that the two metabolic reactions are catalyzed by different forms of the cytochrome P-450 system. 18 references.

001444 Neal, H.; Bond, Ann. Lilly Research Centre Ltd., Erl Wood Manor, Windlesham, Surrey, England **Modification of**

PGO activity by specific uptake inhibitors fluoxetine, nisoxetine and LR5182. *Neuropharmacology*. 18(10):813-819, 1979.

The density of potogeniculocipital (PGO) waves induced by reserpine (PGO/res) in encephale isole cats was reduced by the serotonin uptake inhibitor fluoxetine and by the noradrenaline uptake inhibitor nisoxetine, but not by the preferential dopamine uptake inhibitor LR-5182. These depressions in PGO/res density were antagonized by cyproheptadine. PGO waves induced by the benzoquinoline derivative R04-1284 (PGO/1284) were influenced only by fluoxetine; a depression PGO/1284 could be induced by nisoxetine only in animals pretreated with LR-5182. PGO waves induced by para-chlorophenylalanine (PGO/pcpa) were influenced by all three uptake inhibitors, with fluoxetine the least effective. The nisoxetine-induced depression in PGO/pcpa density was antagonized by phenoxybenzamine, but not by phenolamine. Results suggest that PGO waves are modulated by serotonin and noradrenalin acting independently at separate sites and by dopamine acting indirectly through the noradrenergic control system. 29 references. (Author abstract modified)

001445 Neal, H.; Keane, P. E. Lilly Research Centre Ltd. Erl Wood Manor, Windlesham, Surrey GU20 6PH, England **Electrically and chemically induced spindling and slow waves in the encephale isole rat: a possible role for dopamine in the regulation of electrocortical activity.** *Electroencephalography and Clinical Neurophysiology*. 48(3):318-326, 1980.

The electrocortical effects of electrical and chemical stimulation of brain areas known to contain dopaminergic cell bodies or terminals were studied in encephale isole male Wistar rats. Electrical stimulation of medial basal midbrain areas with single stimuli resulted in a single evoked spindle, while stimulation of more lateral areas resulted in slow waves and spindling. These effects were blocked or reduced by pretreatment with 6-hydroxydopamine. Electrical stimulation of the caudate nucleus produced a single evoked spindle, and local injection of dopamine into the caudate-induced spindling as well as slow waves at high doses. Slow waves were also induced by electrical stimulation of the basal forebrain or injection of dopamine into this area. Results suggest that striatal and limbic dopaminergic pathways may be involved in the production of cortical spindling and slow waves. 42 references.

001446 Nelson, William T., Jr. City University of New York **Effect of morphine on excitability characteristics of CNS reward structures.** (Ph.D. dissertation). Dissertation Abstracts International. 39(8):4091-B. 1979. Ann Arbor, Univ. Microfilms No. 7902550. 492p., 1978.

The effect of morphine on excitability characteristics of CNS reward structures was examined in rats implanted with pairs of bipolar electrodes at two of three sites: locus coeruleus (LC), substantia nigra pars compacta (SNc), and medial forebrain bundle (MFB). LC placements produced intracranial self-stimulation (ICSS) response rates equal to those placed lateral to this structure, but greater than those of placements medial to it. SNc placements produced greater ICSS rates than those placed medially to this structure, but less than rates of placements located in the SNr. MFB placements produced ICSS rates greater than those placed medial of this structure. The C-T functions of the LC, SNc, and MFB placements were similar except at long C-T intervals. LC placements and those just lateral or ventral to LC showed large facilitation under morphine. Dorsal MFB placements showed facilitations, while sites medial to and within MFB showed depressions. Dorsal SN placement yielded facilitations, whereas those ventral within SNc and SNr produced more variability and a tendency toward depressed rates. Effects of naloxone and amphetamine were also examined. (Journal abstract modified)

001447 Nemeroff, Charles B. Biological Sciences Research Center, Dept. of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Neurotensin: persistence an endogenous neuroleptic?** Biological Psychiatry. 15(2):283-302, 1980.

The possibility that neurotensin is an endogenous neuroleptic is explored in rat and calf. Neurotensin (NT), an endogenous tri-decapeptide, is distributed heterogeneously in brain, localized preferentially in the synaptosomal fraction after density gradient centrifugation, and binds to brain membranes reversibly, saturably, and with high affinity. These characteristics along with the demonstration of a Ca dependent release of this neuropeptide from brain slices suggest that this substance is a neuromodulator. Certain properties of NT are compared to neuroleptic agents. The findings support the hypothesis that NT is a neuromodulator. It is a neuropeptide which shares many but not all properties with neuroleptic agents. It is concluded that its role in normal and abnormal behavioral and neurological disease states remains undetermined. 42 references. (Author abstract modified)

001448 Nemeroff, Charles B.; Mason, George A.; Hatley, Ossie L.; Jahnke, Gloria; Prange, Arthur J., Jr. Biological Sciences Research Center, Dept. of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Lack of effect of a behaviorally active dose of cholecystokinin octapeptide upon aromatic amino acid levels in plasma and brain.** Brain Research. 184(2):529-532, 1980.

The possibility that the effects of cholecystokinin (CCK) might be mediated through an alteration in the concentrations of plasma and brain amino acids was investigated in Sprague-Dawley rats injected i.p. with 100mcg/kg bodyweight of CCK octapeptide, a dose sufficient to inhibit tail-pinch-induced feeding by about 90%. The results demonstrate the lack of a significant effect on the ratio of any of these amino acids to the sum of its competitors. Insulin produced a significant rise in plasma and brain tryptophan and reduction of plasma tyrosine. An increase in the plasma ratio of tryptophan to its competitors and a decrease in the plasma ratio of tyrosine to its competitors were both statistically significant in the insulin treated animals. It is concluded that the administration of CCK is not associated with a significant alteration in the concentrations of plasma and brain amino acids. 13 references.

001449 Nemeroff, Charles B.; Osbahr, Albert J., III; Manberg, Paul J.; Ervin, Gregory N.; Prange, Arthur J., Jr. Biological Sciences Research Center, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Alterations in nociception and body temperature after intracisternally administered neurotensin, beta-endorphin, other endogenous peptides and morphine.** (Unpublished paper). Research Report, NIMH Grant MH-32316, 1979. 17 p.

The antinociceptive and hypothermic effects of intracisternal administration of 11 endogenous neuropeptides (including neurotensin and beta-endorphin) and morphine were evaluated in mice. Of the substances tested, neurotensin (NT) and beta-endorphin exerted both significant antinociceptive and hypothermic effects; NT was the most potent in inducing hypothermia whereas beta-endorphin was the most potent antinociceptive agent via this route of administration. Both NT and beta-endorphin were, on a molar basis, considerably more potent antinociceptive agents than morphine, met-enkephalin, or leu-enkephalin. NT-induced analgesia and hypothermia were both found to be significantly dose dependent. Substance-P was found to produce significant hyperalgesia and hyperthermia. Bombesin produced a significant hypothermic effect, whereas somatostatin and luteinizing hormone releasing hormone produced hyperthermia. None of the other peptides studied (bradykinin, thyrotropin

releasing hormone, melanocyte stimulating hormone releasing inhibiting hormone, somatostatin, met-enkephalin, and leu-enkephalin) produced any significant alterations in colonic temperature or response to a noxious stimulus with the doses tested. These data demonstrate that NT and beta-endorphin are quite potent in inducing hypothermia and in producing an antinociceptive state. 28 references. (Author abstract modified)

001450 Nijjar, Mohinder S.; Smith, Thomas L.; Hauser, George. Hauser, Ralph Lowell Laboratories, McLean Hospital, Belmont, MA 02178 **Evidence against dopaminergic and further support for alpha-adrenergic receptor involvement in the pineal phosphatidylinositol effect.** Journal of Neurochemistry. 34(4):813-821, 1980.

Experiments to determine whether dopaminergic receptors are present in the rat pineal gland and to characterize the alpha-receptors are reported. It was found that the stimulation by (-)-norepinephrine of 32Pi incorporation into acidic phospholipids, especially phosphatidylinositol in the rat pineal gland is mediated through alpha-adrenergic receptors. The effects of dopamine, dopaminergic agonists apomorphine and piribedil, and a number of antagonists were studied. From the several lines of evidence it is concluded that only alpha-adrenergic receptors are concerned with the changes in pineal phospholipid metabolism brought about by the various agonists used and that the action of dopamine occurs through these receptors rather than through discrete dopaminergic receptors. 29 references. (Author abstract modified)

001451 Nistico, G.; Di Giorgio, R. M.; Rotiroli, D.; Naccari, F.; Calatroni, A. Institute of Pharmacology, Faculty of Medicine, University of Messina, Messina, Italy **Effects of intraventricular beta-endorphin on GABA system in some areas of chick brain.** Research Communications in Chemical Pathology and Pharmacology. 26(3):469-478, 1979.

The effects of a single dose (10mcg) of beta-endorphin on GABA and free glutamic acid content and on glutamic acid decarboxylase (GAD) and GABA transaminase (GABA-T) activities in the diencephalon, brainstem, and brain hemispheres were examined in chicks with cannula chronically implanted in the third cerebral ventricle. At the time of maximum beta-endorphin-induced behavioral stupor and analgesia, a significant decrease in GABA concentration and a significant increase in GABA-T activity were found in the diencephalon and brainstem. No changes in GAD activity or glutamic acid content were observed. Results suggest that some central effects of beta-endorphin may be due to interference with GABA transmission. (Author abstract modified)

001452 Nitsch, Cordula. Neurobiologische Abteilung, Max-Planck-Institut für Hirnforschung, Deutschordenstrasse 46, D-6000 Frankfurt/M.-71, Germany **Regulation of GABA metabolism in discrete rabbit brain regions under methoxy-pyridoxine -- regional differences in cofactor saturation and the preictal activation of glutamate decarboxylase activity.** Journal of Neurochemistry. 34(4):822-830, 1980.

The activities of the enzymes of the gamma-aminobutyric acid (GABA) system, glutamate decarboxylase (GAD) and GABA-transaminase, were measured in discrete regions of the rabbit brain before the onset and during the course of sustained epileptiform seizures induced by the vitamin B6 analogue methoxy-pyridoxine. Results indicate that only investigation during the preictal period and in regional brain areas can reveal changes specific for the drug and perhaps representing the cause for seizure development, without being masked by additional alterations resulting from the severe functional and metabolic derangement during the ictal events. It was found that a decrease in vivo in

the level of the enzyme product, GABA, is able to activate GAD. 69 references. (Author abstract modified)

001453 Nordberg, Agneta; Wahlstrom, Goran; Larsson, Christer. Department of Pharmacology, University of Uppsala, S-751 23 Uppsala, Sweden **Increased number of muscarinic binding sites in brain following chronic barbiturate treatment to rat.** *Life Sciences*. 26(3):231-237, 1980.

The effects of chronic barbiturate treatment on number of muscarinic binding sites in brain were studied in rats. Rats received as their only drinking fluid a solution of sodium barbital (3.33mg/ml) for more than 40 weeks. In two groups (A3 and A12), the barbital solution was withheld and replaced by water 3 and 12 days before sacrifice. Another group received barbital until sacrifice (B), while a fourth served as untreated controls (C). Synaptosomes from different parts of the brain were incubated with radioactive quinuclidinyl bezilate for 60 min. A significantly increased number of binding sites was found in the striatum and midbrain plus medulla oblongata plus cerebellum of A3 rats in comparison with group C. Saturation studies indicated that group A3 had significantly more receptors in the midbrain plus medulla oblongata plus cerebellum than group C, while there were no differences in receptor affinity. 18 references. (Author abstract modified)

001454 Nowak, J. Z.; Bielkiewicz, B.; Lebrecht, U. Dept. of Biogenic Amines, Institute of Pharmacology, Polish Academy of Sciences, 60, Narutowicza St., 90-136 Lodz, Poland **Dimaprit-induced hypothermia in normal rats: its attenuation by cimetidine and by tricyclic antidepressant drugs.** *Neuropharmacology*. 18(10):783-789, 1979.

Dimaprit (DIM), a highly specific histamine H₂-receptor agonist, induced a dose dependent hypothermia in female Wistar rats. The hypothermic action of DIM (100 and 250mcg) was partially antagonized by cimetidine, a histamine H₂-receptor antagonist, and by the tricyclic antidepressant drugs imipramine and amitriptyline. Results support a role for histamine H₂-receptors in central thermoregulatory mechanisms in the rat. 32 references. (Author abstract modified)

001455 Okajima, Taiichiro; Motomatsu, Toshiharu; Kato, Ken-ichi; Ibayashi, Hiroshi. Third Dept. of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka, Japan **The stimulatory effect of beta-endorphin on the plasma prolactin levels was diminished in the rats treated with 6-hydroxydopamine.** *Life Sciences*. 26(9):699-705, 1980.

It is reported that intraventricular injection of beta-endorphin (beta LPH61-91) in urethane anesthetized male rats led to a dose dependent increase of plasma prolactin levels, but intravenous injection of apomorphine completely abolished the stimulatory effect of beta-endorphin. Animals treated with 6-hydroxydopamine (6-OHDA) and 6-OHDA plus desmethylimipramine showed inhibition of beta-endorphin-induced prolactin release. These results suggest that beta-endorphin presynaptically inhibits the activity of dopaminergic neurons, leading to the stimulation of plasma prolactin levels. 14 references. (Author abstract modified)

001456 Olds, M. E.; Nienhuis, R. Division of Biology 216-76, California Institute of Technology, Pasadena, CA 91125 **Depressant effects of topical morphine on self-stimulation-related units in hypothalamus.** *Neuropharmacology*. 18(10):801-812, 1979.

The effects of locally injected morphine on hypothalamic unit responses correlated with self-stimulation behavior were studied in male rats implanted with probes for self-stimulation in the posterior lateral hypothalamus and substantia nigra. At a concentration of 5mcg/mcl, morphine had small and variable ef-

fects, but repeated applications of the low dose tended to increase the number of units that became excited. At a concentration of 10mcg/mcl, morphine consistently depressed the neuronal firing rate, and repeated injections potentiated the depression. Naloxone (1 or 2mcg/mcl) blocked or attenuated the depressant action of simultaneously injected morphine (10mcg/mcl) and sometimes even produced excitation. Naloxone also excited some units when given alone. Results suggest a direct, specific action of morphine on neural activity related to a central positive reinforcing mechanism. 86 references. (Author abstract modified)

001457 Olney, John W.; de Gubareff, Taisija; Labruyere, Joann. Dept. of Psychiatry, Washington University School of Medicine, 4940 Audubon Avenue, St. Louis, MO 63110 **Alpha-aminoadipate blocks the neurotoxic action of N-methyl aspartate.** *Life Sciences*. 25(6):537-540, 1979.

The excitatory amino acids, glutamate (Glu) and N-methyl aspartate (NMA), were administered subcutaneously to mice in doses sufficient to destroy neurons of the arcuate hypothalamic nucleus (AH). Pretreatment with glutamic acid diethylester (GDEE) or alpha-aminoadipate (alpha-AA), agents proposed as specific antagonists of the excitatory action of Glu and NMA respectively, resulted in suppression by alpha-AA of the neurotoxic activities of both agonists, while GDEE exerted no detectable influence over the neurotoxic actions of either agonist. These findings, with other accumulating evidence, suggest that an excitatory mechanism underlies the neurotoxicity of these agents and that AH neurons may have predominantly aspartergic excitatory inputs. 12 references. (Author abstract)

001458 Olpe, H.-R.; Glatt, A.; Laszlo, J.; Schellenberg, A. CIBA-GEIGY Ltd., Biology Research Laboratory, Pharmaceuticals Division, Basel, Switzerland **Some electrophysiological and pharmacological properties of the cortical, noradrenergic projection of the locus coeruleus in the rat.** *Brain Research*. 186(1):9-19, 1980.

The effect of repetitive stimulation of the locus coeruleus (LC) on the discharge rate of spontaneously active neurons of the visual, rostral and cingulate cortex was investigated in untreated and catecholamine depleted rats. In untreated animals, the inhibitory transsynaptic effects predominated over the excitatory ones. In catecholamine depleted rats, the percentage of inhibited cells was significantly reduced in all areas. The vast majority of spontaneously active neurons in all cortical regions was depressed by microiontophoretically applied noradrenaline (NA). A few cells were resistant to NA; no excitatory effects were noticed on any cell. The transsynaptically mediated depression of the discharge rate of cells in all three cortical areas was reversibly antagonized by the iontophoretically administered beta receptor blocking drug practolol. On the contrary, the alpha receptor blocking drugs piperoxane and WB4101 were ineffective in this respect. Thus, it is tentatively concluded that the NA elicited depression of cells in the cortex is mediated by a receptor of the beta type. 23 references. (Author abstract modified)

001459 Oltmans, G. A.; Olsauskas, R.; Comaty, J. E. Dept. of Pharmacology, University of Health Sciences, Chicago Medical School, Chicago, IL 60612 **Hypothalamic catecholamine systems in genetically obese mice (obob): decreased sensitivity to reserpine treatment.** *Neuropharmacology*. 19(1):25-33, 1980.

Genetically obese C57BL/6J mice showed a significantly decreased sensitivity to reserpine, compared to lean control mice. Reserpine treatment produced significant decreases in the hypothalamic norepinephrine (NE) content in obese mice, but NE levels decreased more slowly and were always significantly

higher in obese mice than in lean mice. The depletion of dopamine (DA) also occurred more slowly in obese mice, but the final degree of depletion did not differ between groups. The DA content of the pituitary and the NE content of several peripheral tissues were depleted equally in obese and lean mice by the reserpine treatment. The incomplete and delayed depletion of hypothalamic catecholamines in obese mice did not appear to result from incomplete distribution of reserpine in the hypothalamus and could not be overcome by high doses of reserpine. Inhibition of NE synthesis did not significantly reduce the amount of NE remaining in the hypothalamus of obese mice after reserpine, indicating the residual NE was not newly synthesized. 28 references. (Author abstract modified)

001460 Ono, T.; Oomura, Y.; Nishino, H.; Sasaki, K.; Muramoto, K.; Yano, I. Dept. of Physiology, Faculty of Medicine, Toyama Medical and Pharmaceutical University, Toyama 930-01, Japan **Morphine and enkephalin effects on hypothalamic glucoreceptive neurons.** Brain Research. 185(1):208-212, 1980.

The effects of morphine and enkephalin on glucose sensitive neurons in the lateral hypothalamic area (LHA) and on glucoreceptor neurons in the ventromedial hypothalamus (VMH) were examined in male Wistar rats. Electrophoretically applied morphine and glucose both produced inhibition in the LHA and excitation in the VMH. The effect of morphine lasted about twice as long as that of glucose, but the magnitude, latency, and dose effects of morphine and glucose were quite similar. Enkephalin produced almost the same effects as morphine. The effects of morphine and enkephalin, but not of glucose, were antagonized by naloxone. Results suggest that enkephalinergic activity in the LHA and VMH may be involved in feeding behavior. 15 references.

001461 Orensanz, Luis M. Departamento de Investigacion Centro Especial Cajal, Carretera de Colmenar Km 9.1, Madrid 34, Spain **High affinity binding of beta-alanine to regions of rat CNS.** Neuropharmacology. 18(11):913-916, 1979.

High affinity binding of beta-alanine to synaptosomal mitochondrial fractions was found in seven regions of male Wistar rat CNS. Dissociation constants ranged from 5 nM in cerebellum to 28 nM in thalamus. Maximal binding capacities varied from 33 p-moles/g in cerebral cortex to 91 p-moles/g in thalamus. 7 references. (Author abstract modified)

001462 Osborne, Hillman; Herz, Albert. Dept. of Neuropharmacology, Max-Planck-Institut für Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany **K-evoked release of met-enkephalin from rat striatum in vitro: effect of putative neurotransmitters and morphine.** Naunyn-Schmiedeberg's Archives of Pharmacology. 310(3):203-209, 1980.

The effects of drugs on the K-evoked release of met-enkephalin from superfused rat striatal slices were investigated using a specific radioimmunoassay. GABA, at concentrations of 50mM and 100mM, and the GABA agonist muscimol significantly inhibited the release. The inhibiting effect of GABA was reversed by picrotoxin suggesting that GABA inhibition is mediated by GABA receptors. Selected concentrations of the dopamine agonists apomorphine and ergonovine, as well as of haloperidol, acetylcholine, carbachol, noradrenaline, glutamic acid and substance-P, had no effect on the release of met-enkephalin. Increases in the evoked release (80%) and striatal enkephalin content (60%) were found in rats after chronic haloperidol administration, pointing to an increase in the synthesis and utilization of striatal enkephalin. No differences were found between the release from slices from morphine tolerant/dependent and naive rats or after addition of naloxone to slices derived from tolerant/dependent animals. Selected concentrations of mor-

phine and naloxone had no effect on release suggesting the absence of mechanism for the regulation of enkephalin release involving autoreceptors. 35 references. (Author abstract)

001463 Owen, F.; Cross, A. J.; Lofthouse, R.; Glover, Vivette. Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow, HA1 3UJ, England **Distribution and inhibition characteristics of human brain monoamine oxidase.** Biochemical Pharmacology. 28(7):1077-1080, 1979.

Monoamine oxidase (MAO) activity was determined postmortem in 14 regions of 10 normal human brains, using 5-hydroxytryptamine (5HT), benzylamine, and tyramine and dopamine as substrates. Regional distribution with 5HT, benzylamine, and tyramine was generally similar with the highest activities observed in the hypothalamus. However, with dopamine as substrate, the highest MAO activity was seen in the nucleus accumbens. The distribution type-A and type-B MAO activities indicated by studies with the different substrates was not always consistent with that suggested by studies with specific MAO inhibitors (clorgyline and deprenyl). 28 references. (Author abstract modified)

001464 Palacios, Jose M.; Young, W. Scott, III; Kuhar, Michael J. Kuhar, Dept. of Pharmacology, Johns Hopkins University School of Medicine, 725 North Wolfe St., Baltimore, MD 21205 **Autoradiographic localization of H1-histamine receptors in brain using 3H-mepyramine: preliminary studies.** European Journal of Pharmacology. 58(3):295-304, 1979.

Tritiated mepyramine (3H-MEP) was used to label H1-histamine receptors in slide mounted tissues from male Sprague-Dawley rat and Hartley guinea-pig brain. The saturable, high affinity binding of 3H-MEP showed drug specificity similar to that observed for H1-receptors in a variety of systems. The association constant and number of binding sites were lower in rat brain than guinea-pig brain. Autoradiographic studies revealed a marked regional variation in receptor density in both species. In guinea-pigs, a high density of H1-receptors was seen in the molecular layer of the cerebellum; in the hippocampal formation, highest densities were in the molecular layer of the dentate gyrus while lower levels were found in the dendritic fields of pyramidal cells. In rats, high levels of H1-receptors were found in the hypothalamus, outer layers of the cerebral cortex, amygdala, superior colliculus, and nucleus tractus solitarius. 32 references. (Author abstract modified)

001465 Palfreyman, Michael G.; Bohlen, Peter; Huot, Sylvie; Mellet, Michel. Centre de Recherche Merrell International 16, rue d'Ankara, F-67084 Strasbourg-Cedex, France **The effect of gamma-vinyl GABA and gamma-acetylenic GABA on the concentration of homocarnosine in brain and CSF of the rat.** Brain Research. 190(1):288-292, 1980.

Using a sensitive and specific HPLC method, the effect of gamma-vinyl GABA and gamma-acetylenic GABA on rat brain and CSF homocarnosine concentrations was examined. It was found that, in addition to the elevation in CSF homocarnosine following acute treatment with gamma-vinyl GABA or chronic treatment with small doses of gamma-acetylenic GABA, the concentrations of homocarnosine in whole brain are markedly elevated. Results suggest that since the correlation between the two parameters, although significant, is not impressive, CSF data can be only of limited usefulness as an indicator of brain levels. It is not entirely clear how the inhibitors of GABA-T cause an increase in the concentrations of homocarnosine, but several possible explanations are offered. It is suggested that since homocarnosine is heterogeneously distributed in different brain areas and produces pharmacological effects when injected i.e.v., it might function as a neurotransmitter. 10 references.

001466 Palmer, G. C. Dept. of Pharmacology, University of South Alabama, College of Medicine, Mobile, AL 36688 **Beta adrenergic receptors mediate adenylate cyclase responses in rat cerebral capillaries**, *Neuropharmacology*, 19(1):17-23, 1980.

The adenylate cyclase system of capillary fractions from rat cerebral cortex was sensitive to activation by the beta-adrenergic agonists isoproterenol, norepinephrine (NE), metaproterenol, tazolol, terbutaline, and dobutamine, in decreasing order of potency. These beta-agonist-induced responses were potently inhibited by propranolol. Only one form of cyclic AMP dependent phosphodiesterase was present in the capillary preparation. Results showed that cerebral capillaries have a mixed population of beta-adrenergic receptors mediating the stimulation of adenylate cyclase. 27 references. (Author abstract modified)

001467 Panula, P. A. J. Dept. of Anatomy, University of Helsinki, Siltavuorenpenger 20A, 00170 Helsinki 17, Finland **A fine structural and histochemical study on the effect of kainic acid on cultured neostriatal cells**, *Brain Research*, 181(1):185-190, 1980.

The effects of kainic acid were examined in cultured rat neostriatal cells. Acetylcholinesterase (AChE) activity did not differ between KA treated and control cultures, and KA did not destroy the fine structure of nerve fibers containing neurotubules and small clear vesicles. These findings are in striking contrast to those reported for in vivo studies and suggest that cultured AChE positive cells may lack the receptor site through which KA exerts its toxic effect. The cells observed in culture may represent a subpopulation of cells that is resistant to KA. 19 references.

001468 Pashko, Steven; Vogel, Wolfgang H. Center for Alcohol Studies, Rutgers University, New Brunswick, NJ 08903 **Factors influencing the plasma levels of amphetamine and its metabolites in catheterized rats**, *Biochemical Pharmacology*, 29(2):221-225, 1980.

Rats fitted with chronically indwelling Silastic tubing catheters in the right jugular vein were given orally a low dose of d-amphetamine sulfate (A) alone or in combination with other chemicals or environmental conditions to investigate factors influencing plasma levels of A and its metabolites. In general, A levels increased slowly over 1 hour, peaked, and declined during the 4 hour test period. Level of metabolites were already appreciable at 15 minutes, slowly increased to 1 hour, and remained constant over the rest of the testing period. A variety of chemicals and environmental conditions that were meant to mimic some human situations (social interaction, food, stress, alcohol, bicarbonate, and ammonium chloride) selectively affected the half-lives, the areas under the time curve, and the levels of A and metabolites at different times during the experiment. In two cases, individual differences in A and metabolite blood levels were found in these rats, which belong to a genetically homogenous group. 11 references. (Author abstract modified)

001469 Patel, I. H.; Levy, R. H. Dept. of Pharmacokinetics and Biopharmaceutics, Hoffman-LaRoche, Inc., Nutley, NJ 07110 **Intramuscular absorption of carbamazepine in rhesus monkeys**, *Epilepsia*, 21(1):103-109, 1980.

The intramuscular absorption characteristics of carbamazepine were investigated in a group of six chair adapted rhesus monkeys from three parenteral formulations: a) 100mg/ml of carbamazepine in PEG-400; b) 50mg/ml of carbamazepine in PEG-400; and c) 50mg/ml of carbamazepine in a PEG-400-Tween-80 mixture (9:1). The absolute bioavailability was determined by administering formulations A or B intravenously. The kinetic profiles obtained after intramuscular administration suggests biphasic absorption in the majority of animals: an initial rapid absorption phase yielding peak concentrations in less than 1 hour

followed by a slower phase where absorption was probably rate limiting. The absolute bioavailability was 38% from formulation A, 81% from formulation B and 82% from formulation C. In two of four cases, Tween-80 eliminated the rate limiting absorption phase. Data suggest that an intramuscular formulation of carbamazepine with acceptable bioavailability may be feasible. 10 references. (Author abstract)

001470 Paul, S. M.; Zatz, M.; Skolnick, P. Clinical Psychobiology Branch, NIMH, Bethesda, MD 20205 **Demonstration of brain-specific benzodiazepine receptors in rat retina**, *Brain Research*, 187(1):243-246, 1980.

The existence of brain specific benzodiazepine receptors in rat retina is demonstrated in a series of experiments. In addition to a brain specific binding site, retinal homogenates contain significant amounts of a peripheral type binding site, which permits simultaneous comparison of these two binding sites in the same tissue. Further evidence for the brain specific nature of the retinal receptor was obtained from study of the potencies of several benzodiazepines in inhibiting (3H)diazepam binding in vitro. Since GABA and GABAergic-like drugs have been demonstrated to increase the affinity of (3H)benzodiazepines for the benzodiazepine receptor in brain, the effects of GABA were studied in washed retinal membrane. The enhancement by GABA of (3H)diazepam binding in retinal membranes was similar to that previously reported for brain. It is suggested that the retina may represent a valuable model for understanding both the physiological functions of the benzodiazepine receptor and the mechanisms of action of the benzodiazepines. 10 references.

001471 Paul, Steven M.; Axelrod, Julius; Saavedra, Juan M.; Skolnick, Phil. Clinical Psychobiology Branch, NIMH, Bethesda, MD 20205 **Estrogen-induced efflux of endogenous catecholamines from the hypothalamus in vitro**, *Brain Research*, 178(2-3):499-505, 1979.

Short-term organ cultures of the intact female Sprague-Dawley rat hypothalamus were used to study the effects of various estrogenic compounds on catecholamine release. Estradiol-17beta (0.1 to 20 mM) produced a concentration dependent efflux of norepinephrine and dopamine, but its biologically inactive enantiomer, estradiol-17beta, was ineffective in concentrations up to 20mM. Diethylstilbestrol, a potent nonsteroidal estrogen, was as effective as estradiol-17beta in inducing catecholamine efflux. Weak and nonestrogenic steroids such as estrone, estriol, and corticosterone were without effect. The time course of the estrogen-induced efflux of hypothalamic catecholamines was similar to that previously reported for the estrogen-induced accumulation of hypothalamic cyclic AMP, providing further evidence for the involvement of catecholamines in this effect. Results suggest that estrogen may facilitate the release of catecholamines within the hypothalamus. 11 references. (Author abstract)

001472 Perlow, Mark J.; Reppert, Steven M.; Boyar, Robert M.; Wyatt, Richard J.; Klein, David C.; Wyatt, Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Daily rhythms in cortisol and melatonin in primate CSF: effects of constant light and dark**, (Unpublished paper), Washington, DC, NIMH, 1980. 14 p.

Cerebrospinal fluid (CSF) was continuously collected from the cisternal-cervical subarachnoid space of chair restrained rhesus monkeys to determine if the rhythm in cortisol is altered when the nocturnal increase in melatonin is blocked by constant light and also if the rhythm in cortisol is changed when the animals are exposed to constant darkness, a condition in which the daily elevation of melatonin is prolonged. Under diurnal lighting, melatonin concentrations were elevated during darkness

and low during illumination. The melatonin rhythm persisted in constant darkness but was suppressed in constant illumination. Under diurnal lighting, cortisol concentrations were elevated in the early portion of the light period. Neither constant illumination nor constant darkness altered the daily rhythmicity, indicating that the daily rhythmicity of melatonin secretion was not responsible for the daily rhythmicity of cortisol secretion in the rhesus monkey. 39 references. (Author abstract modified)

001473 Pert, Agu; Massari, V. John; Tizabi, Yousef; O'Donohue, Thomas L.; Jacobowitz, David. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Effects of 6-hydroxydopamine and 5,7-dihydroxytryptamine brainstem lesions on morphine analgesia in the rat. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 4 p.

The effects of 6-hydroxydopamine lesions to the A-1 catecholamine nuclei and 5,7-dihydroxytryptamine lesions to the brainstem raphe nuclei were evaluated on the analgesic actions of morphine following systemic administration or direct injections into the nucleus gigantocellularis of rats. Although the lesions were effective in decreasing dorsal horn 5-hydroxytryptamine (5-HT) and norepinephrine (NE), 50% and 64% respectively, their effects on morphine analgesia were disappointingly subtle and varied. The findings do not support the hypothesis that the analgesic actions of morphine at supraspinal levels are predominantly determined by the activation of descending NE or 5-HT pathways originating from the brainstem. 15 references. (Author abstract)

001474 Pert, Candace B.; Taylor, Duncan. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Type 1 and type 2 opiate receptors: a subclassification scheme based upon GTP's differential effects on binding. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 4 p.

Evidence for a simple opiate receptor subclassification scheme is presented: type 1 receptor is guanosine triphosphate (GTP) sensitive, adenylate cyclase coupled, and associated with a sodium ionophore; type 2 receptor is GTP resistant and uncoupled. Type 1 receptors were found predominantly in the ileum and in most of rat brain, particularly the areas which mediate analgesia; type 2 receptors predominate in the limbic system, a neuroblastoma glioma cell hybrid, vas deferens, pituitary, and invertebrate nervous systems. Type 1 receptors are easily reversed by naloxone, while type 2 receptors are even resistant to naloxone blockade. Comparisons of a type 1 receptor enriched area (midbrain) and a type 2 receptor enriched area (frontal cortex) revealed the following ligand selectivity (in order of strongest preference for type 1): naloxone, morphine, diprenorphine, N-allylnormetazocine, ketocyclazocine, cyclazocine, beta-endorphin, D-Ala-enkephalin amide, met-enkephalin, leu-enkephalin. Benzomorphans generally lack selectivity but differ in their relative affinity for the type 1 antagonist conformation. 21 references. (Author abstract)

001475 Perumal, A. S.; Murthi, V. K. New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032 **Effect of norepinephrine on chromatin protein phosphorylation in C-6 glioma cells.** Life Sciences. 26(6):447-452, 1980.

The effect of norepinephrine on chromatin protein phosphorylation in rat C-6 glioma cultures was examined. The cultures were exposed to labelled sodium phosphate after treatment with NE with or without propranolol. Histones and nonhistone proteins (NHP) were extracted from chromatin and there was no significant change in the specific activity of the total pool of histones and NHP between control and the other two groups. However, after electrophoretic separation F2a2 histone showed a 60% increase while F2b and F3 histones exhibited a 40% de-

crease in phosphorylation in response to NE. The possible role of beta-receptors on nuclear protein phosphorylation and genomic expression is discussed. 28 references. (Author abstract modified)

001476 Pickles, Hilary G.; Simmonds, M. A. Clinical Pharmacology Unit, Institute of Neurology, Queen Square, London WC1N 3BG, England **Antagonism by penicillin of gamma-aminobutyric acid depolarizations at presynaptic sites in rat olfactory cortex and cuneate nucleus in vitro.** Neuropharmacology. 19(1):35-38, 1980.

GABA and muscimol, superfused over slice preparations of rat olfactory cortex and cuneate nucleus, depolarized the afferent nerve fibers in the lateral olfactory tract and dorsal funiculus, respectively. Penicillin (0.1 to 10mM) caused a reversible, concentration related depression of the GABA and muscimol dose/response curves with no detectable shift of the curves to the right. This pattern of antagonism by penicillin was distinctly different from the antagonism exerted by bicuculline, picrotoxin, and strychnine. Results suggest that penicillin blocks the response mechanism rather than the receptors mediating depolarizations by GABA and muscimol. 16 references. (Author abstract)

001477 Placheta, Peter; Karobath, Manfred. Pharmakologisches Institut, Wahringerstrasse 13a, A-1090, Vienna, Austria **Regional distribution of Na-independent GABA and benzodiazepine binding sites in rat CNS.** Brain Research. 178(2-3):580-583, 1979.

The binding of tritiated GABA and tritiated flunitrazepam was studied in eight regions of the Sprague-Dawley rat brain and spinal cord. High and low affinity GABA binding sites were found in all regions examined. The concentration of GABA binding sites was highest in the cerebellum; intermediate in frontal cortex, olfactory bulb, striatum, and hippocampus; and lowest in medulla and spinal cord. The number of benzodiazepine (BZ) binding sites was highest in frontal cortex, olfactory bulb, and midbrain; intermediate in striatum and cerebellum; and lowest in medulla and spinal cord. There were fewer BZ binding sites than high or low affinity GABA binding sites in all brain areas tested, and the ratio of the densities of BZ and GABA receptors was fairly constant except in the cerebellum. Results suggest that GABA receptors may exist independently of BZ receptors in the cerebellum and possibly in other areas. 9 references.

001478 Pollay, Michael; Stevens, F. A. Neurosurgical Section, University of Oklahoma School of Medicine, Oklahoma City, OK **Blood-brain barrier restoration following cold injury.** Neurological Research. 1(3):239-245, 1980.

Cerebral blood flow (CBF), ^{113m}Indium-diethylenetriaminepentaacetic acid (DTPA), and ^{14C}-glucose extraction were measured simultaneously in rat brain from 2 to 58 days following a thermal insult. In the early stage of a cold-induced lesion (2 days), the blood-brain barrier (BBB) was disrupted with resulting leakage and diffusional loss of both glucose and indium-DTPA. The adjacent nonnecrotic brain showed similar but more subtle changes. In both areas, CBF was markedly reduced. CBF and augmented loss of glucose and indium-DTPA continued in the epicenter of the lesion for up to 58 days postinjury while the BBB function in the brain areas surrounding the lesion returned toward normal. These findings were consistent with observation of disruption of BBB activity and of immature brain capillaries during the reparative period. 18 references. (Author abstract)

001479 Pong, S.-S.; Wang, C. C. Merck Institute for Therapeutic Research, Box 2000, Rahway, NJ 07065 **The specificity of**

high affinity binding of avermectin B1a to mammalian brain. *Neuropharmacology*. 19(3):311-317, 1980.

Evidence is presented that avermectin B1a, an anthelmintic with pharmacological properties of paralyzing nematodes and causing an increase in the release of GABA from rat brain synaptosomes, binds to dog brain synaptosomes with an apparent K_d of 1 to 2 nM. This high affinity binding is saturable and the density of binding sites is estimated at 1.54 pmol/mg protein. The binding is stereospecific and the affinities to the binding sites correlate well with anthelmintic activities. The binding sites are unevenly distributed in the areas of the dog brain and apparently emerge during the first 3 weeks of postnatal development. Although the results suggest that the binding sites may be associated with GABA synapses, the lack of competition between GABA and the drug in their bindings suggests that the drug receptors are not associated with GABA postsynaptic receptors. 26 references. (Author abstract modified)

001480 Portaleone, Paolo; Genazzani, Enrico; Pagnini, Giuseppe; Crispino, Antonio; Di Carlo, Francesco. Institute of Pharmacology, University of Turin, School of Medicine, Corso Raffaello 30, I-10125 Turin, Italy **Interaction of estradiol and 2-hydroxy-estradiol with histamine receptors at hypothalamic level.** *Brain Research*. 187(1):216-220, 1980.

Adenylate cyclase activity in hypothalamic membrane preparations of immature (30 days) and adult (at least 61 days) male and female rats in different hormonal conditions were studied to investigate a hypothesized interaction of estradiol and 2-hydroxy-estradiol with histamine receptors in the hypothalamus. The effect of histamine on the hypothalamic adenylate cyclase activity of intact adults, intact immature, adult males castrated when immature, adult males castrated when immature and treated with estradiol-17 β , and adult females ovariectomized while immature and treated with methyl-testosterone-17 α , were compared. Results support the assumption that histamine is involved in the regulation of gonadotrophins. However, the estrogens, particularly the catechol estrogens, seem to interfere with the histamine receptors at the hypothalamic level in the control of gonadotrophin secretion. 20 references.

001481 Pratt, J.; Jenner, P.; Reynolds, E. H.; Marsden, C. D. University Dept. of Neurology, Institute of Psychiatry, Denmark Hill, London SE5, England **Clonazepam induces decreased serotonergic activity in the mouse brain.** *Neuropharmacology*. 18(10):791-799, 1979.

Clonazepam induced a dose dependent increase in cerebral 5-hydroxytryptamine (5HT), 5-hydroxyindoleacetic acid (5HIAA), and tryptophan levels in male Swiss mice. This effect was not related to a decrease in body temperature caused by the drug. In animals pretreated with a monoamine oxidase inhibitor, clonazepam further elevated both 5HT and 5HIAA levels. Pretreatment with probenecid did not prevent the increase in 5HIAA caused by clonazepam. Clonazepam did not alter the accumulation of 5-hydroxytryptophan following inhibition of central decarboxylase activity, but reduced the depletion of 5HT following inhibition of tryptophan hydroxylase activity. Results indicate that clonazepam increases brain tryptophan without altering 5HT synthesis, decreases 5HT utilization, and inhibits the egress of 5HIAA from the brain. 40 references. (Author abstract modified)

001482 Przegalinski, E.; Bigajska, K.; Siwanowicz, J. Institute of Pharmacology, Polish Academy of Sciences, Smetna 12, 31-343 Krakow, Poland **The effect of some new antidepressants on apomorphine-induced hypothermia in mice.** *Journal of Pharmacy and Pharmacology*. 31(8):560-561, 1979.

The effects of variety of tricyclic antidepressants on apomorphine-induced hypothermia were examined in male albino Swiss mice. Imipramine, desipramine, chlorimipramine, nomifensine, femoxetine, and paroxetine antagonized the hypothermic action of apomorphine, although femoxetine was effective only at the highest dose (20 mg/kg minus 1). Chlorimipramine, nomifensine, and femoxetine produced statistically significant effects only at 15 minutes after apomorphine. Mianserin, trazodone, and pizotifen had no effect on the apomorphine-induced hypothermia. Implications for further research are discussed. 19 references.

001483 Ramana Reddy, S. V.; Yaksh, Tony L. Dept. of Neurological Surgery, Mayo Clinic, Rochester, MN 55901 **Spinal noradrenergic terminal system mediates antinociception.** *Brain Research*. 189(2):391-401, 1980.

The role of the spinal noradrenergic terminal system in antinociception was investigated via intrathecal administration of norepinephrine (NE) into the lumbar subarachnoid space of rats and cats implanted with chronic spinal catheters. The strong, dose dependent, behaviorally defined analgesia obtained appeared to be mediated by an alpha receptor, inasmuch as phenylephrine, but not isoproterenol produced the intrathecal effect. Moreover, the antinociceptive effect of NE was antagonized by the prior systemic or intrathecal administration of phentolamine (an alpha blocker), but was unaffected by pretreatment with propranolol (a beta-blocker). The effect of intrathecal NE was significantly potentiated by prior administration of Lilly 51641 (a monoamine oxidase inhibitor) and protriptyline (a reuptake inhibitor), and was not antagonized by the intrathecal administration of a nonspecific vasodilator, papaverine. The antinociceptive effect of intrathecal NE showed tachyphylaxis following repeated injections. No cross-tolerance between intrathecal NE and morphine was observed, suggesting that the spinal action of morphine is not mediated by spinal noradrenergic terminals. Importantly, naloxone had no effect on the intrathecal NE effect. These data provide further evidence of the modulatory role of a spinal noradrenergic system on the spinal processing of nociceptive transmission. 42 references. (Author abstract modified)

001484 Ramirez, Beatriz U. Laboratory of Neurophysiology, Dept. of Cell Biology, Catholic University of Chile, Casilla 114-D, Santiago, Chile **Neurotrophic regulation of muscle autolytic activity.** *Experimental Neurology*. 67(2):257-264, 1980.

The effect of axoplasmic transport on muscle autolytic activity was investigated. Colchicine, a drug known to interfere with axoplasmic transport, was injected under the epineurium of the hypoglossal nerve and the autolytic activity of the corresponding geniohyoid muscle was measured at different times after drug treatment. A blockade of axoplasmic transport by colchicine produced a significant and reversible increase in muscle autolytic activity. This result suggests that neurogenic molecules play an important role in the regulation of muscle catabolism. 16 references. (Author abstract modified)

001485 Redburn, Dianna A.; Stramler, James; Potter, Lincoln T. Dept. of Neurobiology and Anatomy, University of Texas Medical School, Houston, TX 77025 **Inhibition by reserpine of calcium-dependent release of (3H)norepinephrine from synaptosomes depolarized with potassium or veratridine.** *Biochemical Pharmacology*. 28(13):2091-2094, 1979.

The in vivo reserpine treatment of male Sprague-Dawley rats blocked the evoked release of tritiated norepinephrine (3H-NE) from brain synaptosomes in vitro. The calcium dependent release of 3H-NE after depolarization by 56 mM potassium or 100 μ M veratridine was greatly diminished in rats treated with 5 mg/kg i.p. reserpine. Spontaneous leakage of (3H)NE was increased in the reserpine treated animals. Reserpine had no effect

on uptake or release of labeled GABA. These findings support the hypothesis that vesicular NE constitutes the immediate source of neurotransmitter during chemical transmission. 31 references.

001486 Reddy, S. V. R.; Yaksh, T. L. Dept. of Neurologic Surgery. Mayo Clinic, Rochester, MN 55901 **Antinociceptive effects of lanthanum, neodymium and europium following intrathecal administration.** *Neuropharmacology*. 19(2):181-185, 1980.

The trivalent cations lanthanum, neodymium and europium were found to have a weak, dose dependent antinociceptive effect as measured on hot plate and tail flick following administration into the lumbar subarachnoid space of rats implanted with chronic intrathecal catheters. The effects were limited to the hindlimbs and tail. The lanthanum effect was reversible by intrathecal administration of calcium, but was not altered by intraperitoneal administration of naloxone. In equimolar doses, neodymium and europium were found to be significantly more potent than lanthanum. Doses of lanthanum higher than 1 microM and of neodymium and europium greater than 0.3 microM resulted in significant motor weakness of the lower extremities. 26 references. (Author abstract)

001487 Regan, John W.; Roeske, William R.; Yamamura, Henry I. Dept. of Internal Medicine, Health Sciences Center, University of Arizona, Tucson, AZ 85724 **3H-flunitrazepam binding to bovine retina and the effect of GABA thereon.** *Neuropharmacology*. 19(4):413-414, 1980.

The binding of (3H)flunitrazepam to bovine retina and the effect of GABA on that binding were investigated. Whole retinal homogenates revealed specific, high affinity, and saturable (3H)flunitrazepam binding. In washed membrane preparations, 10 microM GABA caused a dramatic decrease in the Kd (42%). The rank order of potency for the inhibition of (dH)flunitrazepam binding by different benzodiazepines was: clonazepam greater than clobazam greater or equal to Ro 5-4864. These results are supportive for the presence of benzodiazepine receptors in the bovine retina and indicate a likeness with the previously described benzodiazepine receptors of mammalian brain. 7 references. (Author abstract modified)

001488 Reichenhal, E.; Hocherman, S. Neurosurgical Department of the Beilinson Medical Center, Petach-Tiqva, Israel **A critical epileptic area in the cat's cortex and its relation to the cortical columns.** *Electroencephalography and Clinical Neurophysiology*. 47(2):147-152, 1979.

The critical size of active penicillin foci in cat's parietal cortex was determined in two different ways: by gradually enlarging the area of drug application from 0.78 mm² to 3.14 mm² and by reducing the area of the active penicillin focus, using subpial incisions. Results indicate that a critical area of 0.7 mm² is necessary. The possibility that in the parietal cortex a single functional column may be the basic generator unit for interictal spikes is discussed. It is concluded that the size of the critical area is related to the cross-sectional area of a single functional column (this column is not yet determined by parallel anatomical findings) and that inactivation of a given epileptic focus in the cat's cortex may be achieved by cutting layer III of the focus. 8 references. (Author abstract)

001489 Reisine, T. D.; Nagy, J. I.; Beaumont, K.; Fibiger, H. C.; Yamamura, H. I. Dept. of Pharmacology, College of Medicine, University of Arizona Health Sciences Center, Tucson, AZ 85724 **The localization of receptor binding sites in the substantia nigra and striatum of the rat.** *Brain Research*. 177(2):241-252, 1979.

Neurotransmitter receptor binding of five ligands was examined in the striatum, substantia nigra (SN), and frontal cortex of male Wistar rats with unilateral 6-hydroxydopamine (6-OHDA) lesions of the nigrostriatal pathway (NSP) or unilateral kainic acid lesions of the striatum. The 6-OHDA lesions of the NSP reduced tritiated dihydroalprenolol (3H-DHA) and naloxone (3H-Nal) binding by 31% and 28%, respectively, in the striatum but increased 3H-DHA and 3H-Nal binding by 44% and 26% in the frontal cortex. The 6-OHDA lesions did not alter striatal receptor binding for tritiated quinuclidinyl benzilate (3H-QNB), muscimol (3H-Mus), or flunitrazepam (3H-Flu). Similarly, intrastriatal kainic acid injections did not alter striatal receptor binding for 3H-Nal, 3H-Flu, or 3H-Mus. The only alteration in receptor density observed in the lesioned animals was a 43% increase in 3H-Flu binding following 6-OHDA lesions of the NSP. Striatal kainic acid lesions did not alter nigral 3H-QNB or 3H-Flu binding, and 6-OHDA lesions did not alter 3H-QNB or 3H-Nal binding in the SN. Scatchard analysis revealed no change in the affinity of the beta-adrenergic receptor for 3H-DHA or in that of benzodiazepine receptor for 3H-Flu in the lesioned animals. 51 references. (Author abstract modified)

001490 Reynier-Rebuffel, A.-M.; Lacombe, P.; Aubineau, P.; Sercombe, R.; Seylaz, J. Laboratoire de Physiologie et Pathologie cerebrovasculaire, Faculté Lariboisière, St. Louis, 10, Avenue de Verdun, 75010 Paris, France **Multiregional cerebral blood flow changes induced by a cholinomimetic drug.** *European Journal of Pharmacology*. 60(2/3):237-240, 1979.

The effects of the cholinomimetic, parasympathetic drug carbachol on regional cerebral blood flow was tested in rabbits, using the 14C-ethanol tissue sampling technique. Intracarotid injection of carbachol significantly increased blood flow in 6 of 10 structures examined, compared to untreated controls. The flow increases were greater following carbachol alone than the after carbachol in combination with atropine. Muscarinic and nicotinic mechanisms involved in this effect are discussed. 8 references. (Author abstract modified)

001491 Rivot, J. P.; Chaouh, A.; Besson, J. M. Unité de Recherches de Neurophysiologie Pharmacologique de l'INSERM (U 161), 2, rue d'Alesia, F-75014 Paris, France **The influence of naloxone on the C fiber response of dorsal horn neurons and their inhibitory control by raphe magnus stimulation.** *Brain Research*. 176(2):355-364, 1979.

The effects of naloxone on the responses of spinal cord dorsal horn neurons to C-fiber stimulation and on the inhibition of these responses by stimulation of the nucleus raphe magnus (NRM) were examined in 19 intact male Sprague-Dawley rats anesthetized with chloralose. A mean 44% facilitatory effect on responses to C-fibers was observed for 12 of the 19 units examined. A mean 30% reduction of the inhibitory effects of NRM was found for 14 of the 19 units. No clear relationship between the facilitatory effects and the diminution of the efficiency of NRM stimulation was found. Results indicate that naloxone facilitates transmission of noxious messages at the spinal level and that endogenous opioids are involved in the inhibitory mechanisms activated by stimulation of the NRM. 41 references. (Author abstract modified)

001492 Roberts, F.; Hill, R. G.; Osborne, R. H.; Mitchell, J. F. Research Institute, Smith Kline and French Laboratories, Welwyn Garden City, Hertfordshire AL7 1EY, England **The effect of depolarizing potassium concentrations on the efflux of GABA from rat dorsal medulla in vivo and from slices and synaptosomes.** *Brain Research*. 178(2-3):467-477, 1979.

A depolarizing concentration of potassium (40mequiv.) did not alter the efflux of tritiated GABA from the dorsal surface of

adult male Porton rat medulla overlying the dorsal column nuclei or from slices of the dorsal region of the caudal medulla containing dorsal column nuclei. The efflux of (3H)GABA from these slices was increased by electrical stimulation and by veratridine (100mM). The elevated potassium concentration also increased the efflux of both endogenous and labeled GABA from crude synaptosomal preparations of this region, without influencing the efflux of labeled sucrose or leucine. Release from synaptosomes could also be induced with 100mM veratridine. Elevated potassium prevented the increased efflux from slices from 14-day-old rat brain. It is suggested that the astrocytic swelling produced by raised potassium concentration restricts the diffusion of GABA away from depolarized terminals. 38 references. (Author abstract modified)

001493 Robinson, D. S.; Campbell, I. C.; Walker, Margaret; Statham, Nancy J.; Lovenberg, W.; Murphy, D. L. Dept. of Pharmacology, Marshall University School of Medicine, Huntington, WV 25701 **Effects of chronic monoamine oxidase inhibitor treatment of biogenic amine metabolism in rat brain.** *Neuropharmacology*. 18(10):771-776, 1979.

The effects of acute and chronic administration phenelzine and tranylcypromine on male Sprague-Dawley rat brain metabolism were determined. Norepinephrine, dopamine, and 5-hydroxytryptamine levels were highest between 1 and 7 days of treatment and then gradually declined with continued drug administration. An adaptive increase in tryptophan hydroxylase, but not in tyrosine hydroxylase, was associated with chronic phenelzine treatment. Tranylcypromine did not alter tryptophan hydroxylase or tyrosine hydroxylase activities, but was associated with a significant increase in aromatic amino acid decarboxylase activity after 14 and 21 days of treatment. 24 references. (Author abstract modified)

001494 Rogawski, Michael A.; Aghajanian, George K. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Activation of lateral geniculate neurons by norepinephrine: mediation by an alpha-adrenergic receptor.** *Brain Research*. 182(2):345-359, 1980.

Single cell recording and microiontophoretic techniques were used to characterize adrenergic receptors in the vicinity of neurons in the male Sprague-Dawley rat lateral geniculate nucleus (LGN). Application of norepinephrine (NE) at low iontophoretic currents (1 to 15nA) produced a delayed activation of most LGN neurons. This activation was mimicked by epinephrine, phenylephrine, alpha-methylnorepinephrine, dopamine, and isoproterenol in decreasing order of potency. The alpha-antagonists phentolamine, piroxane, and WB-4101 produced a selective, dose dependent, reversible blockade of the response to NE. The beta-antagonist sotalol had weak and variable effects at low currents. The presynaptic alpha-agonist clonidine blocked the response to NE at low currents, but produced a partial activation of some units at high currents. The ability of sympathomimetic amines to activate LGN neurons correlated well with their reported affinities for brain alpha1-adrenoceptors labeled with (3H)WB-4101. It is concluded that NE activates neurons in the LGN via a postsynaptic or alpha1-adrenergic receptor. 56 references. (Author abstract modified)

001495 Roques, Bernard P.; Gacel, Gilles; Fournie-Zaluski, Marie-Claude; Senault, Bernard; Lecomte, Jeanne-Marie. Dept. of Chimie Organique, ERA 613 (CNRS), UER des Sciences Pharmaceutiques et Biologiques, 4 ave. de l'Observatoire, F-75006 Paris, France **Demonstration of the crucial role of the phenylalanine moiety in enkephalin analogues for differential recognition of the mu- and delta-receptors.** *European Journal of Pharmacology*. 60(1):109-110, 1979.

A series of enkephalin analogues was tested for potency in the guinea-pit ileum (mu-receptors) and in the mouse vas deferens (delta-receptors). Results showed that enkephalins can be structurally modified to produce compounds selective for the mu-receptor or the delta-receptor. A complete loss of activity on the mouse vas deferens was obtained by replacing the phenyl ring of the phenylalanine residue with an aliphatic hydrophobic moiety, while activity on guinea-pig ileum was maintained. 5 references.

001496 Roth, Robert H.; Doherty, John D.; Walters, Judith R. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Gamma-hydroxybutyrate: a role in the regulation of central dopaminergic neurons?** *Brain Research*. 189(2):556-560, 1980.

The role of gamma-hydroxybutyrate (GHB) in the regulation of central dopaminergic neurons was investigated via comparison of endogenous levels of GHB in the rat substantia nigra with levels found when the dopamine cells are approximately 50% inhibited by systemic administration of GHB. Results demonstrate that subanesthetic doses of GHB (75 to 150mg/kg) cause significant changes in the firing rates of dopamine cells in the pars compacta substantia nigra, with 150mg/kg GHB lowering dopamine cell unit activity by approximately 50%. These doses also significantly decrease levels of DOPAC in the terminal regions of the nigrostriatal and mesolimbic dopamine systems, consistent with the observed inhibitory effects on dopaminergic unit activity. The concentrations of GHB found in the substantia nigra when these changes in dopamine activity were occurring were approximately 25 times the concentrations found in these brain regions in normal rats. These results are consistent with the possibility that, under conditions which may significantly influence the conversion of GABA to GHB, endogenous levels of GHB could fluctuate rapidly enough to effectively modulate the activity of central dopaminergic neurons. 16 references.

001497 Rotter, A.; Birdsall, N. J. M.; Field, P. M.; Raisman, G. Raisman: Laboratory of Neurobiology, National Institute for Medical Research, Mill Hill, London NW7 1AA, England **Muscarinic receptors in the central nervous system of the rat. II. Distribution of binding of (3H)propylbenzylcholine mustard in the midbrain and hindbrain.** *Brain Research Reviews*. 1(2):167-183, 1979.

The distribution of muscarinic receptors in the male Wistar rat midbrain and hindbrain was studied by counting silver grains in light microscope autoradiographs of the specific (atropine sensitive) binding of (3H)propylbenzylcholine mustard in cryostat sections. High grain counts were found in the basilar pontine nuclei, ventral nuclei of the lateral lemniscus, and facial and hypoglossal nuclei. The motor trigeminal nucleus and nucleus ambiguus had medium counts. The interpeduncular nucleus as a whole had low counts, but two bands of intense staining were found on each side around the entry zone of the bundles of afferent cholinergic fibers from the habenula. Intermediate levels of the binding occurred over the inferior colliculus and superficial and intermediate gray layers of the superior colliculus. The molecular layer of the vestibulocerebellar vermis was also distinctly labeled. 75 references. (Author abstract modified)

001498 Rotter, A.; Birdsall, N. J. M.; Burgen, A. S. V.; Field, P. M.; Hulme, E. C.; Raisman, G. Raisman: Laboratory of Neurobiology, National Institute for Medical Research, Mill Hill, London NW7 1AA, England **Muscarinic receptors in the central nervous system of the rat. I. Technique for autoradiographic localizations of the binding of (3H)propylbenzylcholine**

mustard and its distribution in the forebrain. *Brain Research Reviews*. 1(2):141-165, 1979.

The use of (3H)propylbenzylcholine mustard to study the distribution of the muscarinic receptors in the male Wistar rat forebrain is described. The level of specific binding was high in the external plexiform layer of the olfactory bulb, anterior olfactory nucleus, olfactory tubercle, pyriform cortex, stratum radiatum of the hippocampus, stratum moleculare of the dentate gyrus, lateral amygdaloid nucleus, corticoamygdaloid transition zone, anteroventral thalamic nucleus, hypothalamic supraoptic nucleus, caudate-putamen, nucleus accumbens, and laminae 3 and 6 of the neocortex (parietal region). The density of muscarinic receptors was also high in the choroid plexus of the lateral, but not the third or fourth, ventricles. 101 references.

001499 Rotter, A.; Field, P. M.; Raisman, G. Raisman: Laboratory of Neurobiology, National Institute for Medical Research, Mill Hill, London NW7 1AA, England **Muscarinic receptors in the central nervous system of the rat. III. Postnatal development of binding of (3H)propylbenzylcholine mustard.** *Brain Research Reviews*. 1(2):185-205, 1979.

The postnatal development of brain muscarinic receptors was studied by counting silver grains in light microscope autoradiographs of the specific (atropine sensitive) binding of (3H)propylbenzylcholine mustard in cryostat sections from 1 to 17-day-old female Wistar rats. The density of muscarinic receptors was close to the adult level on the first day of life, when only a small fraction of the adult number of synapses had been formed. Of seven areas studied, the hypoglossal nucleus showed the most precocious muscarinic receptor development and the dentate gyrus the most delayed. Developmental changes in the pattern of receptor distribution are described. 53 references. (Author abstract modified)

001500 Saavedra, Juan M. Section on Pharmacology, Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Brain stem adrenergic neurons participate in the regulation of the stress response and in genetic and experimental hypertension.** (Unpublished paper). Bethesda, MD, NIMH, 1979. 10 p.

Data are presented to show that acute immobilization stress results in increased activity of the adrenaline forming enzyme, phenylethanolamine N-methyltransferase, in discrete areas of the rat brain stem. These changes parallel decreased concentrations of adrenaline in the same areas, suggesting an increased release and/or turnover of adrenaline. Similar changes are present in the brain stem of young, spontaneously hypertensive rats. Changes in adrenaline concentrations occur in some brain stem areas in three other models of hypertension, the neurogenic (sino aortic denervation), mineralocorticoid, and genetic, sodium dependent hypertension. These results strongly suggest that discrete brain stem adrenaline forming neurons participate in the development and maintenance of different forms of hypertension, as well as in the central regulation of the stress response. 22 references. (Author abstract)

001501 Saavedra, Juan M. Section of Pharmacology, Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Brain catecholamines during development of DOCA-salt hypertension in rats.** *Brain Research*. 179(1):121-127, 1979.

The activity of the adrenaline forming enzyme phenylethanolamine-N-methyltransferase (PNMT) and the levels of noradrenaline, dopamine, and adrenaline were determined in selective areas of the male Sprague-Dawley rat brainstem and hypothalamus during the development of hypertension induced by treatment with deoxycorticosterone (DOCA) and sodium chloride. Increases in PNMT activity were restricted to the A1 area and locus coeruleus after 2 weeks of treatment, but were extended

to the A2 area after 9 weeks of DOCA/salt. Adrenaline concentrations were higher in these areas only after 9 weeks of treatment. Noradrenaline levels did not change except in the nucleus tractus commissuralis. Dopamine levels were unchanged at all times and in all structures studied. Results implicate brainstem adrenaline neurons in the central response associated with DOCA/salt hypertension. 24 references. (Author abstract modified)

001502 Saavedra, Juan M.; Del Carmine, Renata. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Increased adrenergic beta-receptor stimulation and phospholipid methylation in pineal gland of spontaneously hypertensive rats.** (Unpublished paper). Bethesda, MD, NIMH, 1980. 1 p.

Data are presented which suggest that peripheral adrenaline might play a role in the release of noradrenaline from sympathetic nerves and that pharmacological manipulations of phospholipid methylation could be used as tools for the study of the biochemical mechanisms of increased beta-adrenergic receptor stimulation in hypertension. Pineal catecholamines (CA) N-acetyltransferase activity (NAT) and phospholipid methylation (PLM) were studied in adult spontaneously hypertensive rats (SHR) and Wistar-Kyoto controls (WKY). The SHR rats showed increased adrenaline, decreased noradrenaline, increased NAT activity, and increased PLM activity. These results are compatible with increased uptake of circulating adrenaline and increased release of noradrenaline in the pineal gland of the SHR rats. The increased NAT activity represents increased beta-receptor stimulation. The increased methylation of membrane phospholipids results in translocation of membrane phospholipids, parallels the receptor stimulations, and could represent a biochemical mechanism for increasing receptor-adenylate cyclase coupling through a decrease in membrane viscosity. (Author abstract modified)

001503 Saavedra, Juan M.; Del Carmine, Renata; McCarty, Richard; Guicheney, Pascale; Weise, Virginia; Iwai, Junichi. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Increased adrenal catecholamines in salt sensitive, genetically hypertensive rats (Dahl rats).** (Unpublished paper). Bethesda, MD, NIMH, 1980. 18 p.

Catecholamine levels and activity of catecholamine forming enzymes were quantitated in adrenal glands of Dahl sodium resistant (SR) and sodium sensitive (SS), genetically hypertensive rats, maintained on low salt or high salt diets. A high salt diet resulted in markedly different changes in the catecholamine metabolism in SR and SS rats. In SR rats, a high salt diet reduced the activities of tyrosine hydroxylase (TH) and dopamine-beta-hydroxylase (DBH) as well as the levels of all catecholamines (dopamine, noradrenaline, and adrenaline). In contrast, SS rats fed a high salt diet showed increased TH and phenylethanolamine-N-methyltransferase activities as well as an increased content of adrenal noradrenaline and adrenaline. These findings demonstrate a genetic difference in the effects of a high salt diet on the synthesis of catecholamines in the adrenal gland of Dahl SR and SS rats. Hypertension only occurs in SS rats on a high salt diet, concomitant with large increases in the formation of adrenal catecholamines. 32 references. (Author abstract modified)

001504 Saavedra, Juan M.; Torda, Tichomir. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Increased brain stem and decreased hypothalamic adrenaline-forming enzyme after acute and repeated immobilization stress in the rat.** (Unpublished paper). Bethesda, MD, NIMH, 1979. 18 p.

The effects of immobilization stress on the activity of the adrenaline forming enzyme, phenylethanolamine N-methyltrans-

ferase (PNMT), have been studied in discrete areas of the rat brainstem and hypothalamus. The changes in brain PNMT activity varied with the duration of the stress, were localized to a few brain areas, and the direction of the change varied with the area considered. PNMT was increased after acute immobilization in several areas of the brainstem: A2 area, the anterior part of the nucleus tractus solitarius, and the locus coeruleus. After 7 days of stress, significantly increased PNMT activity was found only in the A2 area and in the cerebellum. In the anterior hypothalamic nucleus, immobilization stress repeated for 7 days resulted in a significant decrease in methyltransferase activity. These results implicate discrete, localized adrenaline forming neurons in the central regulation of the stress response. 37 references. (Author abstract)

001505 Salomon, Raphael; Behar, Leah. Dept. of Neurobiology, Weizmann Institute of Science, Rehovot, Israel **The effect of halogenated amphetamines on protein synthesis in newborn rats.** *Biochemical Pharmacology*. 29(3):335-339, 1980.

The effects of p-chloroamphetamine (PCA) and fenfluramine (Fen) on protein synthesis were studied in newborn rats. Proteins from brain and limb muscles were analyzed by acrylamide SDS gel electrophoresis. Several major proteins detected by this procedure showed a reduced synthesis induced by the drugs. The most noted effect was in a 34K polypeptide that is more abundant in muscle than brain. This polypeptide, as well as a 32K polypeptide, is probably plasma membrane associated. However, the synthesis of only one of these two polypeptides was affected by the halogenated amphetamines. Tropomyosin is similar in size to the 34K polypeptide, therefore a possible identity between these two proteins was investigated. A small difference in size and a distinct pattern of the peptides resulting from these proteins, by partial digestion, excluded such identity. Additionally, a single dose of 10 to 20mg/kg PCA or Fen caused a significant retardation in weight gain within 3 days after treatment, and treated animals were unable to overcome this induced difference in weight even during the following 4 weeks. The possibility of similar effects in humans is discussed. 19 references. (Author abstract)

001506 Samanin, R.; Mennini, T.; Ferraris, A.; Bendotti, C.; Borsini, F. Istituto di Ricerche Farmacologiche Eritrea 62, I-20157 Milan, Italy **Hyper- and hypersensitivity of central serotonin receptors: (3H)serotonin binding and functional studies in the rat.** *Brain Research*. 189(2):449-457, 1980.

The effect of repeated treatment with D-fenfluramine, a serotonin releaser, or methergoline, a serotonin antagonist, on (3H)5-HT binding was studied in various rat brain areas. In animals with the same pretreatments, the anorectic activity of m-chlorophenylpiperazine, a serotonin agonist, was investigated. A 14 day treatment with D-fenfluramine caused a significant decrease in the number of (3H)5-HT binding sites (Bmax) in the diencephalon. A reduction of binding sites was found in the cortex too when D-fenfluramine was administered for 28 days. Methergoline caused no changes of (3H)5-HT binding in any brain area examined when given for 14 days but 28 day treatment led to a significant increase in the striatum, hippocampus and cortex. D-fenfluramine and methergoline cause, respectively, a decrease and increase in the effect of m-chlorophenylpiperazine on food intake. The data indicate that central 5-HT receptor numbers and sensitivity may change after repeated treatments with drugs acting on brain serotonin. 36 references. (Author abstract)

001507 Sanberg, Paul R. Dept. of Behavioural Biology, Research School of Biological Sciences, Australian National University, Canberra City, ACT 2600, Australia **Haloperidol-in-**

duced catalepsy is mediated by postsynaptic dopamine receptors. *Nature*. 284(5755):472-473, 1980.

The cataleptic effects of haloperidol were examined in 10 male Wistar hooded rats using kainic acid and cortical ablation to destroy postsynaptic and presynaptic dopamine receptors respectively. Because previous studies have unavoidably damaged both pre and postsynaptic striatal dopamine receptors, it has not been known whether these two receptors are separately involved in neuroleptic-induced catalepsy. The present study demonstrates that the cataleptic effects of haloperidol area apparently mediated by dopamine receptors localized postsynaptically on striatal neurones. 16 references.

001508 Sanberg, Paul R.; Lehmann, John; Fibiger, Hans C. Fibiger: Div. of Neurological Sciences, Dept. of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Sedative effects of apomorphine in an animal model of Huntington's disease.** *Archives of Neurology*. 36(6):349-350, 1979.

The sedative effectiveness of apomorphine in a newly developed animal model of Huntington's disease was examined. The motor responses of rats with kainic acid lesions of the neostriatum to a sedative dose of apomorphine was similar to that observed in intact controls. In contrast, compared to controls, a marked potentiation of the motor stimulant effects of dextroamphetamine was confirmed in the kainic acid lesioned group. It is suggested that the pathological changes underlying the symptoms observed in this animal model and in Huntington's disease do not include abnormalities in presynaptic dopamine receptors in the neostriatum. 11 references. (Author abstract)

001509 Sangde, Chaichan; Franz, Donald N. Franz: Dept. of Pharmacology, University of Utah, College of Medicine, Salt Lake City, UT 84132 **Lithium enhancement of central 5-HT transmission induced by 5-HT precursors.** *Biological Psychiatry*. 15(1):59-75, 1980.

The effects of acute and chronic lithium chloride administration on synaptic transmission between bulbospinal norepinephrine or 5-hydroxytryptamine (5-HT) pathways and sympathetic preganglionic neurons were tested in unanesthetized, spinal cats. Discharges recorded from sympathetic preganglionic white rami were evoked by stimulation of spinal reflex pathways or descending excitatory pathways in the cervical spinal cord. Acute lithium administration produced insignificant depression of the reflex pathway but markedly depressed transmission through the intraspinal pathway, an effect that was prevented by depletion or blockage of 5-HT. These observations and the failure of lithium to alter the typical effects of L-dopa on both pathways indicate that lithium does not affect transmission through the excitatory NE pathway. L-tryptophan alone produced little or no depression of either pathway, but 3 to 4 hours after lithium, this dose of L-tryptophan gradually depressed transmission through both pathways by about 20%. After chronic lithium pretreatment, L-tryptophan rapidly depressed transmission through spinal reflex and intraspinal pathways by 40% and 50%, respectively. Chronic lithium pretreatment also more than doubled the depression of transmission through both pathways produced by 30mg/kg of 5-HTP. The average of plasma lithium levels 8 to 10 hours after the last chronic dose was 1.5meq/l. These results support the proposal that lithium increases the uptake of L-tryptophan and 5-HTP by central 5-HTP terminals, and thereby enhances 5-HT synthesis which is reflected in increased transmission at central 5-HT synapses. 48 references. (Author abstract)

001510 Sano, Kenji; Noshiro, Osamu; Katsuda, Kimio; Nishikori, Koji; Maeno, Hiroo. Dept. of Pharmacology and Biochemistry, Central Research Laboratories, Yamanouchi Pharmaceuti-

cal Co., Ltd., Itabashi-ku, Tokyo 174, Japan **Dopamine receptors and dopamine-sensitive adenylate cyclase in canine caudate nucleus.** *Biochemical Pharmacology*. 28(24):3617-3627, 1979.

The relationship between (3H)dopamine (DA) binding and DA sensitive adenylate cyclase was examined in canine caudate nucleus. The activities of adenylate cyclase and DA binding showed a similar subcellular distribution, and were present primarily in the synaptic membrane functions. Binding of DA to crude synaptic membranes was rapid, saturable, and reversible in the presence of 2mM ATP. The equilibrium dissociation constant (Kd) for the binding was about 1.5mM, almost identical to the Kd of adenylate cyclase for DA to stimulate half maximally. Binding of DA in the absence of ATP exhibited a negative cooperativity which was abolished by addition of 2mM ATP. DA binding in the presence of 2mM ATP and DA sensitive adenylate cyclase in the membranes were affected in a similar manner by catecholamines, some antidepressants, and a variety of neuroleptics, with the exception of some phenothiazine derivatives such as chlorpromazine and fluphenazine. Propranolol and cocaine did not inhibit either activity. DA sensitivity of the particulate adenylate cyclase tended to be increased by .001% Lubrol PX in incubation but was greatly impaired by more than .005%. 35 references. (Author abstract modified)

001511 Sargent, William Q.; Simpson, John R.; Beard, James D. Department of Physiology and Biophysics, University of Tennessee Center for the Health Sciences, Memphis, TN 38104 **Renal response of ethanol-treated dogs to increased filtered loads of sodium, bicarbonate, and chloride.** *Toxicology and Applied Pharmacology*. 51(2):303-310, 1979.

The renal response in ethanol treated and control dogs to marked elevations in the filtered loads of the major extracellular anions, chloride and bicarbonate, was studied. An attenuated natriuresis and bicarbonaturia was found in ethanol treated animals during the hypertonic sodium bicarbonate infusion. Known effectors of sodium bicarbonate reabsorption, i.e., volume status, pCO₂, potassium stores, and filtration rate were not different between ethanol treated and untreated animals. It is concluded that ethanol pretreatment ameliorated the depressant effect of the sodium bicarbonate infusion on tubular reabsorption. 16 references. (Author abstract modified)

001512 Sato, Hitomi; Sakamoto, Yoshimasa; Kamei, Chiaki; Shimizu, Masanao. Dept. of Child Health, Faculty of Science of Living, Osaka City University, Osaka, Japan **EEG activity changes in juvenile rats chronically treated with phenobarbital.** *Folia Psychiatrica et Neurologica Japonica*. 33(3):323-327, 1979.

EEG activity changes in juvenile rats chronically treated with phenobarbital were investigated in 32 male Wistar HLA rats. Results indicate that dosages of phenobarbital which induced no symptoms clinically, caused the slowing up of EEG background activities in rats. These changes occurred gradually after 2 to 3 weeks of dosage administration. Furthermore, in the 50mg/kg/day group, beta waves significantly increased after 8 weeks and there were changes in the theta and delta waves. Results support the theory that some pathological changes, either reversible or irreversible, occur in the CNS through long treatment with barbiturates. 4 references.

001513 Satoh, Masamichi; Amano, Hiro; Nakazawa, Takahiro; Takagi, Hiroshi. Dept. of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606, Japan **Inhibition by calcium of analgesia induced by intracisternal injection of porcine calcitonin in mice.** *Research Communications in Chemical Pathology and Pharmacology*. 26(1):213-216, 1979.

The analgesia induced by intracisternal injections of 3.0U porcine calcitonin or by 0.5mcg morphine in male dd-K mice was

reduced by simultaneous intracisternal injections of calcium chloride (0.1mcmol). However, porcine calcitonin in doses up to 0.96U had no analgesic effects when microinjected into the nucleus reticularis gigantocellularis of rats, which is highly sensitive to morphine. These findings suggest that calcium is involved in the analgesic actions of both calcitonin and morphine but acts through different mechanisms. 10 references.

001514 Satoh, Masamichi; Kawajiri, Shin-ichi; Ukai, Yojiro; Yamamoto, Masaki. Dept. of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606, Japan **Selective and non-selective inhibition by enkephalins and noradrenaline of nociceptive response of lamina V type neurons in the spinal dorsal horn of the rabbit.** *Brain Research*. 177(2):384-387, 1979.

The effects of microiontophoretically applied methionine-enkephalin, leucine-enkephalin, and noradrenaline (NA) on nociceptive and nonnociceptive responses in lamina-V type neurons of the dorsal horn were compared in male albino rabbits. When applied preferentially to the proximal dendritic region of the lamina-V type neurons, both enkephalins significantly inhibited bradykinin (BK) induced activity in 25 of 31 neurons, but did not alter tactile-induced activity. The inhibitory action of the enkephalins on the nociceptive response was blocked by naloxone in 6 of 8 neurons. NA suppressed activity induced by BK and by tactile stimulation, but the NA-induced inhibition was not blocked by naloxone. Results indicate that the enkephalins act through specific opiate receptors to selectively inhibit the response of lamina-V type neurons to noxious stimulation. 12 references.

001515 Satoh, T.; Fukumori, R.; Nakagawa, I.; Minegishi, A.; Kitagawa, H.; Yanaura, S. Department of Biochemical Pharmacology, Faculty of Pharmaceutical Sciences, Chiba University, Yayoi-cho 1-33, Chiba, Japan **The effects of pyrazole and chlorpromazine on the anticonvulsant action of tryptophol in mice.** *Research Communications in Psychology, Psychiatry and Behavior*. 4(3):285-297, 1979.

The effects of tryptophol (TOL) on the pentylenetetrazol (PTZ) induced seizures was studied in male mice. Pretreatment of mice with pyrazole, an inhibitor of liver alcohol dehydrogenase (ADH), apparently increased brain TOL level and strongly potentiated the anticonvulsant action of TOL. In contrast, pretreatment with chlorpromazine (CPZ), an inhibitor of brain aldehyde reductase, reduced the anticonvulsant action of TOL, which suggested that CPZ suppressed the effect of TOL by inhibiting the conversion of TOL to indoleacetaldehyde (IAald) in the brain. It was concluded that TOL must be converted to IAald in the brain for the manifestation of the anticonvulsant effect of TOL. 18 references. (Author abstract modified)

001516 Sawynok, J.; Labella, F. S.; Pinsky, C. Dept. of Pharmacology and Therapeutics, University of Manitoba, 770 Bannatyne Avenue, Winnipeg, Manitoba, R3E 0W3 Canada **Effects of morphine and naloxone on the K-stimulated release of methionine-enkephalin from slices of rat corpus striatum.** *Brain Research*. 189(2):483-493, 1980.

The effects of morphine and naloxone on the K stimulated release of methionine-enkephalin (ME) released from superfused slices of rat corpus striatum were investigated via radioimmunoassay (RIA). The basal release of 2.5 plus or minus 0.2 pM/g/min was increased approximately three fold upon exposure of tissue to 30mM K for 5 minutes. This increase in release was not observed in the absence of Ca²⁺. Both morphine and (-)naloxone significantly depressed the release of ME evoked by 30mM K but did not alter basal release. The (D) isomer of naloxone, which lacks opiate antagonist activity, did not affect basal

or evoked release. A consistent depression of release was not observed when 47 mM K was used to evoke the release of ME. The issue of whether a feedback mechanism controls the release of ME from the striatum cannot be resolved until it is known whether the effect of morphine and naloxone on ME release are mediated by opiate or nonopiate mechanisms. 58 references. (Author abstract modified)

001517 Scarnati, E.; Forchetti, C.; Ciancarelli, G.; Pacitti, C.; Agnoli, A. Dept. of Human Physiology, School of Medicine, University, I-67100 L'Aquila, Italy **Responsiveness of nigral neurons to the stimulation of striatal dopaminergic receptors in the rat.** *Life Sciences*. 26(15):1203-1209, 1980.

The microinfusion of low doses of apomorphine into the striatum of anesthetized rats was used to examine the responsiveness of nigral neurons to the stimulation of striatal dopaminergic receptors in the rat. The electrical activity of the neurons of the substantia nigra pars compacta was depressed. The infusion of bromocriptine had an excitatory or inhibitory effect. These data suggest that: 1) the action of the two dopamine agonists on the striatonigral pathway is different; 2) the striatum might contain dopaminergic receptors located on cells projected to the substantia nigra with different roles in the feedback regulation of the latter; and 3) the inhibitory action of systemically injected apomorphine is not simply due to a stimulation of dopamine mediated by fibers descending from the striatum to the substantia nigra. 26 references. (Author abstract modified)

001518 Scatton, Bernard; Bartholini, Giuseppe. Synthelabo (LERS), 31, Avenue Paul-Vaillant Couturier, F-92220 Bagneux, France **Modulation by GABA of cholinergic transmission in the striatum.** *Brain Research*. 183(1):211-216, 1980.

Systemic administration of the GABA mimetic agents muscimol and alpha-(chloro-4-phenyl) fluoro-5-hydroxy-2-benzilidene-amino-4-butyramide increased the acetylcholine (ACh) content of the male Sprague-Dawley rat striatum. This effect persisted after unilateral 6-hydroxydopamine lesions, indicating it was not dependent on the integrity of the nigrostriatal dopaminergic pathway. In the lesioned animals, the elevation of ACh by muscimol was antagonized by concomitant treatment with picrotoxin. Results provide evidence for a direct GABA mediated inhibitory influence on cholinergic cells which is intrinsic to the striatum. 27 references.

001519 Schaefer, Andras; Komlos, Marta; Seregi, Andras. Institute of Experimental Medicine, Hungarian Academy of Sciences, 1450 Budapest 9, P.O.B. 67, Hungary **Studies on the effect of catecholamines and chelating agents on the synaptic membrane Na,K-ATPase activity in the presence and absence of hydroxylamine.** *Biochemical Pharmacology*. 28(15):2307-2312, 1979.

Noradrenaline, dopamine, and the metal chelators ethylenediaminetetraacetate (EDTA) and ethyleneglycol-bis-(beta-aminoethyl ether)-N,N-tetraacetic acid (EGTA) stimulated the sodium postassium dependent adenosine triphosphatase (Na,K-ATPase) activity in synaptic membranes from CFY rat brain by reversing inhibition caused by a metal contaminant in ATP. The effects of all four compounds increased in the presence of hydroxylamine. The stimulatory effect of EGTA was eliminated by an excess of calcium (Ca²⁺), but the effect of EDTA was only reduced. The Na,K-ATPase activity could be stimulated by dopamine in the presence of EGTA bound by excess Ca²⁺, but not in the presence of EDTA and excess Ca²⁺. When an ATP supply free of the inhibitory contaminant was used, hydroxylamine strongly inhibited Na,K-ATPase activity, and this inhibition could be reversed by catecholamines and chelating agents. Phenoxybenzamine, chlorpromazine, haloperidol, and phentolamine prevented or reduced the catecholamine stim-

ulation of Na,K-ATPase activity without altering basal activity when a metal contaminated supply ATP was used, but inhibited the Na,K-ATPase activity when ATP free of inhibitory metal was used. 46 references. (Author abstract modified)

001520 Schainker, B. A.; Cicero, T. J. Dept. of Psychiatry, Washington University School of Medicine, St. Louis, MO 63110 **Acute central stimulation of luteinizing hormone by parentally administered N-methyl-D,L-aspartic acid in the male rat.** *Brain Research*. 184(2):425-437, 1980.

The physiological activity, site of action, and toxicity of N-methyl-D,L-aspartic acid (NMA), a potent neuroexcitatory and neurotoxic glutamic acid analogue, were investigated. NMA acutely elevates serum luteinizing hormone (LH) in male rats when given subcutaneously in doses below those that cause morphologically detectable hypothalamic neurotoxicity. NMA treatment in doses known to be subtoxic by morphological criteria fails to induce any permanent neuroendocrine dysfunction as assessed by several physiological parameters. Like naloxone, NMA elevates serum LH by reversibly stimulating a central labile pool. Neither has a direct stimulatory effect on the pituitary in vitro. Neither NMA nor naloxone is dependent upon testosterone for its LH stimulatory action and both increase serum LH through physiological mechanisms responsive to testosterone inhibition. It is concluded that subtoxic LH stimulating doses of NMA provide a useful tool in discerning neurotransmitter systems involved in central control of the hypothalamic pituitary gonadal axis. 27 references. (Author abstract modified)

001521 Schmidt, John T.; Freeman, John A. Dept. of Anatomy, Vanderbilt University School of Medicine, Nashville, TN 37232 **Electrophysiologic evidence that retinotectal synaptic transmission in the goldfish is nicotinic cholinergic.** *Brain Research*. 187(1):129-142, 1980.

The effect of various pharmacological agents on the synaptic efficacy of each of three classes of goldfish retinotectal fibers was assessed by the use of current source density analysis, and implications for the hypothesized nicotinic cholinergic nature of retinotectal synaptic transmission are discussed. All six different nicotinic antagonists were effective in decreasing the responses of all three fiber classes to a criterion level: alpha-bungarotoxin, allopurinol, curare, metocurine, hexamethonium, and gallamine. Atropine, a muscarinic antagonist had only a slight effect. Five nicotinic agonists tested also decreased synaptic responses: nicotine, carbamylcholine, acetylcholine, succinyl choline, and decamethonium, presumably via cellular depolarization and receptor desensitization. Two inhibitors of acetylcholinesterase prolonged the response at one dose and decreased it at another. Hemicholinium 3, an inhibitor of the high affinity uptake of choline, produced a gradual activity dependent decrement in the responses. Beta-bungarotoxin, a presynaptically acting toxin, abolished not only the postsynaptic components but also the presynaptic components. In all other cases, the presynaptic deflections were generally unaffected, and with the exception of the toxins, a return to at least 90% of the control value was achieved. In contrast, GABA and bicuculline both produced no discernible effect on the three classes of responses, and glutamate produced only a slight decrement, which probably represents a nonspecific effect. 40 references. (Author abstract modified)

001522 Schmidt, Michael J. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Dopamine agonist-induced hyperglycemia in rats: effects of lergotril mesylate.** *European Journal of Pharmacology*. 59(1/2):95-101, 1979.

In fasted male Sprague-Dawley rats, the direct acting dopamine agonists lergotril and apomorphine caused marked hyper-

glycemia, but compounds that release endogenous dopamine (amphetamine and methylphenidate) or inhibit dopamine reuptake (LR5182) failed to elevate blood glucose. The effect of lergotril was dose dependent, causing blood glucose to rise three-fold above resting levels at 5mg/kg i.p. Blood glucose increased prior to the onset of the behavioral signs of dopamine stimulation. The effect of lergotril was attenuated by phentolamine, propranolol, or butaclamol, and was prevented by adrenalectomy. Data indicate that all compounds with dopaminergic effects do not produce hyperglycemia. Results suggest that the action of lergotril may be indirect, possibly mediated by the release of catecholamines from the adrenal glands. 28 references. (Author abstract modified)

001523 Schubert, D.; LaCorbiere, M.; Klier, F. G.; Steinbach, J. H. Neurobiology Dept, Salk Institute, P.O. Box 1809, San Diego, CA 92112 **The modulation of neurotransmitter synthesis by steroid hormones and insulin.** *Brain Research.* 190(1):67-79, 1980.

The effects of steroid hormones and insulin on neurotransmitter synthesis in PC12 cells (10% fetal calf and 5% horse serum) and the effects of glucocorticoids on the morphology of intracellular dense core vesicles were examined. Glucocorticoids stimulate tyrosine hydroxylase activity and catecholamine synthesis, while markedly inhibiting acetylcholine synthesis and storage in a clone of sympathetic nerve-like cells. Nerve growth factor enhances the effect of glucocorticoids on tyrosine hydroxylase. The steroid effect is specific for glucocorticoids. Concomitant with the shift in neurotransmitter synthesis, there is an increase in the mean diameter of intracellular dense core vesicles. In contrast to glucocorticoids, insulin increases the specific activity of choline acetyltransferase through the interaction with typical insulin receptors. 32 references. (Author abstract modified)

001524 Schuberth, Jan; Dahlberg, Leif. National Laboratory of Forensic Chemistry, University Hospital, 581 85 Linköping, Sweden **Antagonistic effects of isovalerate and glycine on plasma choline levels in rabbits.** *Life Sciences.* 26(4):273-276, 1980.

The effects of isovalerate and glycine on plasma choline levels were examined in the rabbit. Infusion into rabbits of glycine increased the concentration of plasma choline, while infusion of neutralized isovaleric acid which conjugates glycine caused decreased levels. It is suggested that these effects are due to differences in the availability of glycine, convertible into serine which subsequently displaces choline from phospholipids in the base exchange reaction. Possible antidotal effects of glycine on the neurological symptoms precipitated by isovaleric acid are noted. 14 references. (Author abstract modified)

001525 Schwartzkroin, Philip A.; Prince, David A. Prince: Dept. of Neurology, Stanford University, Stanford, CA 94305 **Changes in excitatory and inhibitory synaptic potentials leading to epileptogenic activity.** *Brain Research.* 183(1):61-77, 1980.

The effects of penicillin, an epileptogenic agent, and bicuculline, a GABA antagonist, on excitatory and inhibitory postsynaptic potentials (EPSPs and IPSPs) were studied in the guinea-pig hippocampal slice preparation. Neither substance enhanced monosynaptic EPSP amplitude in CA1 pyramidal cells, but both agents depressed IPSPs. Large depolarizations that gave rise to cellular bursting activity developed when either agent was added to the bathing medium. An increase in the incidence of fast prepotentials or d-spikes was also observed. Results suggest that penicillin and bicuculline block cellular IPSPs and consequently allow remote intrinsic excitatory events to invade the cell soma and trigger action potentials. 56 references. (Author abstract modified)

001526 Seiler, N.; Bink, G.; Grove, J. Centre de Recherche Merrell International, 16, rue d'Ankara, F-67084 Strasbourg, Cedex, France **Relationships between GABA and polyamines in developing rat brain.** *Neuropharmacology.* 19(3):251-258, 1980.

To study the relationships between GABA and polyamines in developing rat brain the levels of GABA were increased in rat brains during postnatal development by treatment with 4-aminohex-5-enoic acid, a specific enzyme activated inhibitor of GABA aminotransferase. The GABA rate increase followed the developmental increase of glutamate decarboxylase, but there was a substantial net increase of brain GABA levels even at day 3 and their net increase at day 10 was as great as in a mature brain. Elevation of brain GABA in 25-day-old Ss was accompanied by a 50% decrease of S-adenosylmethionine decarboxylase activity. The effects of GABA aminotransferase inhibitors, bicuculline, muscimol were also determined. It appears that glia formation in rat brain is most active between days 10 and 22 of postnatal life. The overall results indicate that observed changes in the polyamine biosynthetic enzymes occur preferentially in the glial compartment of the brain. 58 references. (Author abstract modified)

001527 Serra, G.; Argiolas, A.; Klimek, V.; Fadda, F.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Chronic treatment with antidepressants prevents the inhibitory effect of small doses of apomorphine on dopamine synthesis and motor activity.** *Life Sciences.* 25(5):415-424, 1979.

The effects of apomorphine on rats were examined. In control rats, small doses of apomorphine decreased motor activity and reduced 3,4-dihydroxyphenylacetic acid content in the caudate nucleus. A larger dose increased motor activity and elicited stereotypy. Chronic treatment with imipramine, amitriptyline, and mianserin counteracted or reversed the effect of small doses of apomorphine on motor activity and potentiated the central stimulant response to the larger dose of apomorphine. Changes in apomorphine responses were observed after 10 but not after 2 days of imipramine treatment and persisted unaltered up to 4 days after imipramine withdrawal. It is suggested that chronic treatment with antidepressants induces persistent subsensitivity in presynaptic dopamine receptors. The relevance of the findings in the therapeutic effect of these drugs is discussed. 22 references. (Author abstract modified)

001528 Sershen, H.; Lajtha, A. Center for Neurochemistry, Rockland Research Institute, Ward's Island, NY 10035 **The effect of nicotine on the metabolism of brain proteins.** *Neuropharmacology.* 18(10):763-766, 1979.

The effects of nicotine on protein synthesis were determined in immature and adult mouse brain. In adult brain slices, the incorporation of valine into protein was stimulated by incubation with L-nicotine, decreased by D-nicotine, and unaltered by nicotinic acid or nicotinamide. A tendency toward increased incorporation was seen in adults treated in vivo with nicotine, but the increase was not significant. In newborn brain slices, the incorporation of valine into protein was significantly inhibited by nicotine both in vivo and in vitro. 13 references. (Author abstract modified)

001529 Shah, Ravindra M.; Donaldson, David; Burdett, David. Faculty of Dentistry, University of British Columbia, Vancouver, British Columbia, Canada **Teratogenic effects of diazepam in the hamster.** *Canadian Journal of Physiology and Pharmacology.* 57(6):556-561, 1979.

Pregnant hamsters were treated with different doses of oral and intravenous diazepam during the period of organogenesis. Teratogenic effects of diazepam were observed following oral treatment on days 8 and 10 and following intravenous treatment

on day 11 of gestation. Types of malformations included cleft palate, exencephaly, limb anomalies, and hemorrhage. A dose effect relationship was not observed. Comparison with reported literature seems to indicate that diazepam may be a mild teratogen in some species. 41 references. (Author abstract)

001530 Shani, J.; Goldhaber, G.; Ziv, G. Dept. of Pharmacology, School of Pharmacy, Hebrew University, POB 12065, Jerusalem, Israel Biphase prolactin release by haloperidol and perphenazine in lactating and pregnant cows and ewes. *Biochemical Pharmacology*. 28(7):1213-1215, 1979.

Single intramuscular injections of haloperidol or perphenazine to lactating or nonlactating (pregnant) cows and ewes resulted in biphasic or multiphasic elevation of serum prolactin in most of the treated animals. A rise in serum prolactin was observed 1 to 4 hours after drug administration, with perphenazine yielding a higher and sharper increase than haloperidol, especially in nonlactating animals. A second prolactin peak was observed within 3 to 9 days of treatment in 65% of the haloperidol treated animals and 21% of the perphenazine treated animals. A third peak was seen at an even later state in 15% of the haloperidol treated animals; no third peak was seen in perphenazine treated animals. Results indicate that exhaustion of pituitary prolactin is more profound after perphenazine than after haloperidol. 15 references. (Author abstract modified)

001531 Sharkawi, M. Dept. de pharmacologie, Faculte de medecine, Universite de Montreal, Case Postale 6128, Montreal, Quebec, Canada H3C 3J7 Pharmacological and metabolic interactions between ethanol and the dopamine-beta-hydroxylase inhibitor FLA 63 in mice. *Neuropharmacology*. 19(3):277-280, 1980.

Evidence is presented that the duration of ethanol-induced loss of righting reflex is significantly prolonged in mice pretreated with dopamine-beta-hydroxylase inhibitor FLA 63. The disappearance of ethanol from blood, brain, liver, and kidneys from FLA 63 treatment is significantly delayed as compared to control mice. In vitro, FLA 63 inhibits the activity of mouse liver alcohol dehydrogenase. These results demonstrate that FLA 63 can alter the disposition of ethanol. Consequently, its pharmacological activity is altered. The interpretation of results from experiments in which FLA 63 is employed with other drugs should not be based solely on its inhibitory action of dopamine-beta-hydroxylase. 12 references. (Author abstract modified)

001532 Sherman, Jack Edward. Dept. of Psychology, University of California, Los Angeles, CA 90024 The effects of conditioning and novelty on the rat's analgesic and pyretic responses to morphine. *Learning and Motivation*. 10(4):383-418, 1979.

Six experiments with rats investigated the role of conditioning in morphine tolerance using concurrent assessments of body temperature and pain sensitivity. Experience with morphine produced tolerance to its analgesic effects but enhancement of its hyperthermic effects. Environmental novelty enhanced analgesia, but not body temperature. Under conditions in which a discriminated hyperthermic conditioned response (CR) provided clear evidence that morphine environment learning had developed, discriminated analgesic tolerance was not obtained. Similarly, whereas placebo administrations extinguished the hyperthermic CR, analgesic tolerance remained unaffected. These experiments suggest that the pyretic and analgesic systems are differentially sensitive to conditioning and the effects of novelty. 31 references. (Author abstract modified)

001533 Sherratt, R. M.; Bostock, H.; Sears, T. A. Sobell Dept. of Neurophysiology, Institute of Neurology, National Hospital, Queen Square, London WC1N 3BG, England Effects of 4-aminopyridine on normal and demyelinated mammalian nerve fibres.

Nature. 283(5747):570-572, 1980.

The effects of 4-aminopyridine (4AP) on normal and demyelinated mammalian nerve fibres were investigated. It was previously found that 4AP strongly potentiates transmitter release from the unmyelinated terminals of rat motor nerves, and the possibility arose that demyelinated axon membrane, which can conduct impulses continuously like an unmyelinated fiber, might respond to 4AP. Data indicate that both tetraethylammonium chloride (TEA) and 4AP prolong action potentials of demyelinated and unmyelinated fibers, and both facilitate conduction in fibers blocked by demyelination. It is noted that 4AP is effective at lower concentrations, and has greater promise for clinical use in symptomatic treatment of multiple sclerosis, Eaton/Lambert syndrome, and myasthenia gravis. 11 references. (Author abstract modified)

001534 Sherry, Clifford J.; Hunter, P. Scott. Department of Biology, Texas A & M University, College Station, TX 77843 Long lasting behavioral seizures in the young chicken induced by varying dose levels of phencyclidine. *Research Communications in Psychology, Psychiatry and Behavior*. 4(3):269-275, 1979.

Detailed quantitative observations of the tonic and clonic seizures induced by phencyclidine (PCP) were obtained in the young chick as a first step in determining the effect of PCP in an immature animal lacking a functional neocortex. Findings showed that the effective dose 50% for PCP-induced seizures in the 2-day-old chick is 7.6mg/kg. The lethal dose 50% is 43.58mg/kg. Clonic seizures reach a peak at 4 days of age, when the chick spends approximately 1,276 seconds in clonic seizures. Tonic seizures peak at 3 days, the seizures lasting about 840 seconds. In chicks older than 2 days, the average length of tonic seizures tended to increase while the average time between tonic seizures decreased. It is concluded that this model might provide a simple, inexpensive means of determining the subcortical site(s) of action of PCP and to determine how PCP interacts with other psychotropic agents and neurohumors. 8 references. (Author abstract modified)

001535 Siddik, Zahid H.; Barnes, Roger D.; Dring, L. Graham; Smith, Robert L.; Williams, R. Tecwyn. Laboratory of Toxicology, National Cancer Institute, NIH, Bethesda, MD 20205 The fate of lysergic acid di(14C)ethylamide ((14C)LSD) in the rat, guinea pig and rhesus monkey and of (14C)iso-LSD in rat. *Biochemical Pharmacology*. 28(20):3093-3101, 1979.

The metabolism and elimination of 14C-labeled lysergic acid diethylamide (LSD) were examined in the female Wistar rat, Dunkin-Hartley guinea-pig, and rhesus monkey. Rats given a 1mg/kg i.p. dose of LSD excreted 73% of the 14C in feces, 16% in urine, and 3.4% in expired air as 14CO₂ in 96 hours. Guinea-pigs similarly dosed excreted 40% in feces, 28% in urine, and 18% in expired air. Rhesus monkeys given 0.15mg/kg LSD intramuscularly eliminated 39% of the 14C in urine and 23% in feces. Extensive biliary excretion of 14C LSD occurred in rat and guinea-pig. In all three species, (14C)LSD was almost completely metabolized and little unchanged drug was excreted. Important species differences in the nature and amounts of metabolites were found, however. In rat and guinea-pig, the major metabolites were the glucuronic acid conjugates of 13-hydroxy-LSD and 14-hydroxy-LSD. These metabolites were present in only small amounts in monkey urine, which contained at least nine metabolites of LSD. 16 references. (Author abstract modified)

001536 Siemens, Albert J.; Walczak, Donna; Buckley, Florence E. Research Institute on Alcoholism, Buffalo, NY 14203 Characterization of blood disappearance and tissue distribution of

(3H)cannabidiol. *Biochemical Pharmacology*. 29(3):462-464, 1980.

Two experiments were conducted in the rat to characterize the disappearance of (3H)cannabidiol (CBD) and total (3H) from the blood during the 24 hr after administration and to evaluate the disappearance of (3H)CBD and 3H from blood, liver, and brain from 21.5 to 84 hr after administration, respectively. Intragastric administration resulted in rapid appearance of unchanged (3H)CBD in the blood with a maximum concentration occurring at 2 hr; maximum concentrations of 3H were not reached until 4 to 6 hrs whether blood was analyzed fresh or dried. Disappearance of total 3H was more rapid when based on dry compared to fresh blood. Disappearance of unchanged (3H)CBD from the blood following iv injection was described by a multiexponential function: initial distribution phase was very rapid, while terminal disappearance occurred much more slowly. Unchanged (3H)CBD was present in neck blood at 21.5 hr after administration but could not be detected at 40 to 48 hr, in brain at low levels at 21.5 hrs but not by 40 hr, and in liver for up to 84 hr. The liver showed much higher drug levels than blood or brain at all time points. Drying tissue samples before analysis decreased concentrations of 3H in brain and liver throughout the 84 hr experiment; however, metabolites were present in both organs up to 84 hr. 16 references.

001537 Sievers, J.; Klemm, H. P.; Jenner, S.; Baumgarten, H. G.; Berry, M. Dept. of Neuroanatomy, University of Hamburg, Martinistrasse 52, D-2000 Hamburg 20, Germany Neuronal and extraneuronal effects of intracisternally administered 6-hydroxydopamine on the developing rat brain. *Journal of Neurochemistry*. 34(4):765-771, 1980.

The effects of intracisternal injection of high doses of 6-hydroxydopamine (6-OHDA) to newborn rats were studied. Permanent defects of the monoaminergic neuron system and also of extraneuronal tissue elements were found. The long noradrenergic fiber tracts were irreversibly destroyed, while the short projections recovered and regenerated after a transient period of injury. In the major noradrenergic cell group, the locus coeruleus, most of the cells in the caudal and middle parts degenerated, while a small dorsostral group survived and formed the source of the regenerating fibers. Dopaminergic and serotonergic fiber tracts were also damaged granule and glial cells of the cerebellar cortex as well as the mesenchymal cells of the pial coverings of the cerebellum leading to primitive foliation, absence of fissuration, and defective migration of granule cells and resulting in a marked reduction of cerebellar size, area, and granule cell number. 22 references. (Author abstract modified)

001538 Silverberg, Gerald D.; Ross, Gordon; Corbin, Steven D.; New, William. Division of Neurosurgery, Stanford University Medical Center, 300 Pasteur Drive, Stanford, CA 94305 Time course of serotonin-induced vasoconstriction. *Neurosurgery*. 4(6):539-542, 1979.

Canine cerebral arterial segments tested in a tissue bath escaped from the vasoconstrictor effects of serotonin, and this escape was more rapid in the basilar segments than in the middle cerebral segments. At low doses (0.00000001M), serotonin caused a small prolonged contraction, but a more forceful phasic response was seen at higher doses. Verapamil blocked the phasic portion of the response, but not the low amplitude sustained portion. Increasing the bath concentration of potassium, barium, and tetraethylammonium markedly enhanced the constrictor response of low serotonin doses and significantly inhibited escape. Potentiation of the force and duration of vasoactive amine-induced arterial constriction by small increments of extracellular potassium may be important in the prolonged vascular

narrowing associated with subarachnoid hemorrhage. 21 references. (Author abstract modified)

001539 Simmonds, M. A. Dept. of Pharmacology, School of Pharmacy, 29/39 Brunswick Square, London WC1N 1AX, England Evidence that bicuculline and picrotoxin act at separate sites to antagonize gamma-aminobutyric acid in rat cuneate nucleus. *Neuropharmacology*. 19(1):39-45, 1980.

Bicuculline and picrotoxin were compared over a wide range of concentrations as antagonists of GABA and muscimol. The two antagonists caused an approximately parallel displacement of the agonist dose response curves constructed from depolarizing responses of afferent nerve terminals in the rat cuneate nucleus slice. Schild plots for both antagonists had significantly lower slopes when GABA was used as the agonist, probably due to the influence of GABA uptake processes. The degree of antagonism obtained with combinations of bicuculline and picrotoxin indicated that these two antagonists were acting at independent sites. It is concluded that bicuculline antagonizes GABA and muscimol competitively at the receptor, whereas picrotoxin acts at some stage in the depolarization response mechanism. 25 references. (Author abstract modified)

001540 Simonovic, Miljana; Meltzer, Herbert Y. Dept. of Psychiatry, University of Chicago Pritzker School of Medicine, Chicago, IL 60637 Repeated administration of 5-methoxy-N,N-dimethyltryptamine to male rats potentiates stimulation of prolactin secretion by serotonin agonists. *European Journal of Pharmacology*. 58(4):399-405, 1979.

Repeated administration of the serotonin agonist 5-methoxy-N,N-dimethyltryptamine (5MeODMT, four injections of 5mg/kg each at 3-hour intervals) potentiated the drug's prolactin (PRL) releasing effect. The 5MeODMT pretreatment also enhanced the PRL releasing effects of two other serotonin agonists, quipazine and N,N-dimethyltryptamine, but had no effect on the PRL response to antidopaminergic drugs. The onset of enhanced PRL response to serotonin agonists was gradual and appeared to be due to sensitization of the serotonergic mechanism involved in the regulation of PRL secretion. 28 references. (Author abstract modified)

001541 Skirboll, L. R.; Bunney, B. S. Bunney, B. S. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06610 The effects of acute and chronic haloperidol treatment on spontaneously firing neurons in the caudate nucleus of the rat. *Life Sciences*. 25(16):1419-1433, 1979.

The effects of acute and chronic systemic administration of haloperidol (HAL) on the firing rate and number of spontaneously active type-1 and type-2 neurons in the male Sprague-Dawley rat caudate nucleus were determined. Responses of the two units differed from each other following acute or chronic treatment. Supersensitive responses to ionophoretic dopamine (DA) were found in type-1 units during chronic (22 days) HAL treatment and 1 week after drug termination. However, acute or chronic administration of HAL did not block the inhibitory effects of ionophoretic DA on these neurons. Results support the view that DA postsynaptic supersensitivity is involved in the pathogenesis of tardive dyskinesia, but raise questions concerning the mechanism by which HAL induces this effect. 34 references. (Author abstract modified)

001542 Sloviter, Robert Seth. Pennsylvania State University Serotonin neuropharmacology: behavior and hippocampal electrophysiology. (Ph.D. dissertation). Dissertation Abstracts International. 39(8):3792-B, 1979. Ann Arbor, Univ. Microfilms No. 7902650, 115p., 1978.

The degree to which a number of psychoactive drugs interact with central serotonin receptors was studied in the rat. Behavioral studies using levodopa, amphetamine, LSD, 5-methoxy-N,N-dimethyltryptamine, and p-chlorophenylalanine suggested that stimulation of central serotonin receptors may be a causative factor in drug-induced hallucinations and psychosis. Electrophysiological studies on the hippocampal formation indicated that electrical stimulation of serotonin containing neurons in the midbrain increased the normal excitation of hippocampal granule cells by coincident cortical stimulation. This effect is probably mediated by serotonin receptors, since a serotonin receptor agonist mimicked and a serotonin receptor blocker partially prevented the effect. (Journal abstract modified)

001543 Smellie, F. W.; Daily, J. W.; Wells, J. N. Laboratory of Bioorganic Chemistry, National Institute of Arthritis, Metabolism, and Digestive Diseases, NIH, Bethesda, MD 20205 1-isoamyl-3-isobutylxanthine: a remarkably potent agent for the potentiation of norepinephrine, histamine, and adenosine-elicited accumulations of cyclic AMP in brain slices. *Life Sciences*. 25(22):1917-1924, 1979.

It is reported that 1-isoamyl-3-isobutylxanthine potentiates by two to six fold the accumulations of cyclic AMP elicited in guinea pig cerebral cortical slices by norepinephrine, histamine, and adenosine. The results of experimentation indicate that 1-isoamyl-3-isobutylxanthine is an extremely potent and effective inhibitor of phosphodiesterases involved in the regulation of cyclic AMP levels in guinea pig cerebral cortical slices. The 1-benzyl, 1-isoamyl, and 1-isobutyl derivatives of 3-isobutylxanthine potentiate the accumulation of cyclic AMP elicited by adenosine, while the 1-methyl derivative and 1-isoamyl-3-methylxanthine are inhibitory undoubtedly because of blockade of adenosine receptors by these compounds. It is suggested that xanthines with bulky 1-substituents and 3-substituents appear to be relatively weak adenosine antagonists and relatively specific and potent agents for inhibition of phosphodiesterases involved in cyclic AMP metabolism in brain tissues. 16 references. (Author abstract modified)

001544 Smith, David J.; Pekoe, Gary M.; Martin, Louis L.; Coalgate, Barbara. Dept. of Anesthesiology, West Virginia University Medical Center, Morgantown, WV 26506 The interaction of ketamine with the opiate receptor. *Life Sciences*. 26(10):789-795, 1980.

The interaction of ketamine with opiate receptors in rats was explored. The analgesic effect of the anesthetic agent ketamine HCl is inhibited in rats by the narcotic receptor antagonist naloxone. Racemic (plus and/or minus) ketamine HCl also displaced 3H-naloxone in an opiate receptor binding assay. The potency of ketamine in the assay was reduced nearly six fold by sodium, suggesting that the drug interacts as an agonist. However, some activity as an antagonist was not ruled out. The interaction of ketamine HCl with the opiate receptor was stereospecific with the () salt being more effective than the (-) salt. The stereoselective nature of the interaction is consistent with other studies demonstrating that () ketamine HCl has a greater analgesic effect than the (-) salt. 17 references. (Author abstract modified)

001545 Smith, Thomas L.; Hauser, George. Ralph Lowell Laboratories, McLean Hospital, Belmont, MA 02178 Tricyclic antidepressants and imidazolines as inhibitors of the alpha-adrenergic receptor mediated stimulation of phosphatidylinositol turnover in rat pineal gland. *Biochemical Pharmacology*. 28(11):1759-1763, 1979.

The effects of tricyclic antidepressants and imidazolines on the phosphoinositide effect were studied in vitro in intact rat

pineal glands. Earlier studies with the rat pineal gland have shown that norepinephrine stimulates the incorporation of ^{32}P into phosphatidylinositol through activation of postsynaptic alpha-adrenergic receptors. This response was inhibited by tricyclics and imidazolines. Amitriptyline and oxytazoline displaced the dose/response curve for norepinephrine to the right in a parallel manner indicative of competitive inhibition by these two classes of drugs. 28 references. (Author abstract modified)

001546 Snead, O. C., III; Bearden, L. J.; Pegram, V. Dept. of Pediatrics, University of Alabama, Birmingham, AL 35233 Effect of acute and chronic anticonvulsant administration on endogenous gamma-hydroxybutyrate in rat brain. *Neuropharmacology*. 19(1):47-52, 1980.

The effects of acute and chronic administration of ethosuximide, trimethadione, sodium valproate, clonazepam, phenobarbital, and diazepam on male Sprague-Dawley rat brain concentrations of gamma-hydroxybutyrate (GHB) were determined by gas/liquid chromatography. Acute administration of ethosuximide, trimethadione, or sodium valproate produced an increase in whole brain GHB. Ethosuximide, trimethadione, and phenobarbital decreased whole brain GHB when given chronically. All changes took place in the subcortex and cerebellum. The acute drug-induced changes coincided with the onset of anticonvulsant effects but were short-lived; in the case of ethosuximide and trimethadione, the increase was followed by a significant depression of GHB concentration. 35 references. (Author abstract modified)

001547 Snyder, E. W.; Shearer, D. E.; Beck, E. C.; Dustman, R. E. Neuropsychology Research (151 A), Veterans Administration Medical Center, Salt Lake City, UT 84148 Naloxone-induced electrographic seizures in the primate. *Psychopharmacology*. 67(3):211-214, 1980.

Electrographic seizure activity was recorded shortly following naloxone injections in artificially ventilated, methadone treated stump tailed macaques. Plasma methadone concentrations prior to seizure activity were many times higher than those that have produced respiratory depression and death in nonventilated monkeys. The duration of seizure activity was clearly related to the dose of naloxone. Naloxone was without epileptogenic properties in animals that had not been pretreated with methadone. Results suggest that methadone and naloxone have additive epileptogenic properties when high blood levels of methadone are achieved in the artificially ventilated primate. Naloxone was devoid of antagonistic properties with respect to opiate-induced electroencephalographic spiking activity. 26 references. (Author abstract)

001548 Somana, Reon; Walberg, Fred. Anatomical Institute, University of Oslo, Oslo 1, Norway A re-examination of the cerebellar projections from the gracile, main and external cuneate nuclei in the cat. *Brain Research*. 186(1):33-42, 1980.

Cerebellar projections from the dorsal column and external cuneate nuclei in the cat were studied by means of retrograde axonal transport of horseradish peroxidase. Localized injections covering the entire cerebellar cortex and nuclei showed that the gracile nucleus has a weak projection only to the cortex of the anterior lobe, but that there is a conspicuous projection from the main cuneate nucleus to the cerebellum. Most of these fibers reach lobule V and the adjacent parts of lobules IV and VI, and there is also a heavy projection to the paramedian lobule. Some fibers reach lobule IX and possibly also lobules II, III, and VIIIB, and nuclear afferents also reach the fastigial and interpositus nuclei. Three cerebellar cortical regions are the main targets for the fibers from the external cuneate nucleus, viz. lobule V with the adjacent regions of lobules IV VI, lobules I and II and

lobule IX (the anterior part). Other important afferent regions are the paramedian lobule and the cerebellar nuclei, especially the anterior interpositus, and some fibers reach the flocculus. The projections are predominantly ipsilateral. The findings are discussed in relation to previous experimental observations. 13 references. (Author abstract modified)

001549 Soubrie, P.; Thiebot, M. H.; Jobert, A.; Montastruc, J. L.; Hery, F.; Hamon, M. INSERM V 114, College de France, 11, place Morcelin Berthelot, F-75231 Paris Cedex 05, France **Decreased convulsant potency of picrotoxin and pentetrazol and enhanced (3H)flunitrazepam cortical binding following stressful manipulations in rats.** *Brain Research.* 189(2):505-517, 1980.

Decreased convulsant potency of picrotoxin and pentetrazol and enhanced (3H)flunitrazepam cortical binding following stressful manipulations in rats were investigated. Various stressful manipulations in rats (cold water swim, electric foot shock administration, impaired access to food reward) were found to reduce the convulsant potency of drugs which interfere with GABA or benzodiazepine central processes. The convulsant threshold dosages of picrotoxin or pentetrazol administered after the stress by infusion via a vein of the tail were enhanced. The onset of generalized seizures induced by isoniazid or by thiosemicarbazide was delayed after cold water swim. However, convulsant threshold dosages of bemegride or strychnine perfused at 2 and 0.2 mg/ml, respectively, were not changed by stress. Cold water swim increased the number of cortical (but not cerebellar) (3H)flunitrazepam binding sites (24%) but failed to alter cortical (3H) muscimol binding. This poststress enhancement of binding sites, although suppressed by bicuculline seems not to be dependent on GABAergic mechanisms. Indeed cold water stress did not reduce the ability of muscimol and GABA to increase flunitrazepam binding. Finally, this poststress enhancement of benzodiazepine binding was not found to be paralleled by changes in the protective effects of diazepam against picrotoxin or pentetrazol-induced seizures. 35 references. (Author abstract modified)

001550 Sparks, David L.; Buckholtz, Neil S. Dept. of Biochemistry, Medical University of South Carolina, 171 Ashley Ave., Charleston, SC 29403 **Effects of 6-methoxy-1,2,3,4-tetrahydro-beta-carboline (6-MeO-THbetaC) on audiogenic seizures in DBA/2J mice.** *Pharmacology Biochemistry and Behavior.* 12(1):119-124, 1980.

The time course and dose response effects of 6-methoxy-1,2,3,4-tetrahydro-beta-carboline (6-MeO-THbetaC) for blockage of audiogenic seizures (AGS) in DBA/2J mice were determined. Drugs sharing common effects with 6-MeO-THbetaC were also tested. At a dose of 100mg/kg, 6-MeO-THbetaC blocked AGS between 10 minutes and 12 hours after injection, with maximal inhibition at 1 hour, at which time a dose related decrease in AGS was also demonstrated. All of the drugs tested with blocked AGS, including 6-MeO-THbetaC, THbetaC, 5-hydroxytryptophan, chlorimipramine, and pargyline, have biochemical similarities, suggesting that facilitating serotonin function may be responsible for seizure attenuating effects. 39 references. (Author abstract modified)

001551 Speeg, K. V., Jr.; Wang, S.; Avant, G. R.; Berman, M. L.; Schenker, S. V.A. Medical Center, 1310 24th Ave. South, Nashville, TN 37203 **Antagonism of benzodiazepine binding in brain by antilirium, benzyl alcohol, and physostigmine.** *Journal of Neurochemistry.* 34(4):856-865, 1980.

The effects of the constituents of antilirium upon benzodiazepine binding to brain homogenates were examined to determine why antilirium reverses effectively the narcosis induced by diazepam. Both benzyl alcohol and eserine were found to inhibit

(3H)-diazepam binding to rat brain in a dose dependent manner. Scatchard analysis of inhibition of benzodiazepine binding by benzyl alcohol revealed loss of binding sites and change in equilibrium dissociation constant. No inhibition of labeled ligand binding to the GABA, opiate, muscarinic acetylcholine, or beta-adrenergic receptors was found. Eserine was found to be a more potent inhibitor at the benzodiazepine receptor than benzyl alcohol, but also much less specific, inhibiting binding of labeled ligand to the GABA, opiate, and muscarinic acetylcholine receptors. It is suggested that the inhibition of benzodiazepine binding to brain in vitro by antilirium and its constituents, eserine and benzyl alcohol, may be the explanation, at least in part, for the reversal of diazepam-induced narcosis in vivo, without postulating a cholinergic mechanism for the in vivo effect. 19 references. (Author abstract modified)

001552 Speth, Robert C.; Bresolin, Nereo; Yamamura, Henry I. Yamamura: Dept. of Pharmacology, University of Arizona, Health Sciences Center, Tucson, AZ 85724 **Acute diazepam administration produces rapid increases in brain benzodiazepine receptor density.** *European Journal of Pharmacology.* 59(1/2):159-160, 1979.

In vitro measurement of tritiated flunitrazepam binding revealed a highly significant (139%) increase in the density of brain benzodiazepine receptors in male Sprague-Dawley rats treated acutely with diazepam (50mg/kg i.p.). The increase in receptor density occurred as soon as 15 minutes after the diazepam injection, was dose dependent, and was apparent in the cortex, midbrain/diencephalon, and cerebellum. Phenobarbital, phenytoin, and morphine sulfate did not produce comparable changes in benzodiazepine receptor density. Results suggest that benzodiazepine receptors in brain have an extremely rapid turnover rate or that spare receptors can be rapidly mobilized in response to receptor saturation with a benzodiazepine. 5 references.

001553 Stanley, Michael; Wilk, Sherwin. Department of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Acute and chronic effects of haloperidol and clozapine on dopamine metabolism in two dopamine rich areas of the rat brain.** *Research Communications in Psychology, Psychiatry and Behavior.* 5(1):37-47, 1980.

The acute and chronic effects of the classical antipsychotic drug haloperidol and the atypical antipsychotic clozapine were evaluated by measuring their effects on dopamine (DA) turnover in the rat striatum and tuberculum olfactorium (TO). Chronic administration of a supramaximal dose of haloperidol resulted in a significant decrease in DA turnover in both the striatum and the TO when compared with the effects of acute treatment. Chronic treatment with a maximal dose of clozapine failed to cause a significant reduction in DA turnover in either region when compared with its acute effects on DA turnover. Doses of haloperidol or clozapine which caused a half maximal increase in DA turnover failed to produce significant differences between chronic and acute treatments. 16 references. (Author abstract modified)

001554 Stanton, Toni L.; Winokur, Andrew; Beckman, Alexander L. Alfred I. duPont Institute, P. O. Box 269, Wilmington, DE 19899 **Reversal of natural CNS depression by TRH action in the hippocampus.** *Brain Research.* 181(2):470-475, 1980.

The effects of thyrotropin releasing hormone (TRH) on golden mantled ground squirrels in deep hibernation were examined. Microinjection of TRH into the hippocampus in doses as low as 0.1ng produced a complete transition from hibernation to euthermia, characterized by a large increase in metabolic rate and rapid rise in body temperature. This transition was not ob-

served when TRH was microinjected into the cortex or lateral region of the preoptic/anterior hypothalamic area. The ability of TRH to produce full arousal from a state of deep hibernation when injected into hippocampus is consistent with previous observations of its analeptic properties in reversing drug-induced CNS depression. 24 references.

001555 Stefanis, C. N.; Issidorides, M. R. Dept. of Psychiatry, Athens University, Eginition Hospital, 74 Vas. Sophias Avenue, Athens, Greece **Short and long-term effects of neuroleptics in relation to their cellular mechanism of action.** *Progress in Neuro-Psychopharmacology*. 3(1-3):259-269, 1979.

The short-term and long-term effect of neuroleptics are reviewed in relation to their cellular mechanism of action -- the effects on synaptic transmission and on chromatin. Research literature on the effects of neuroleptics at the synaptic level which supports the currently prevailing dopamine hypothesis is reviewed. Studies of the mechanisms and sites of action of neuroleptics on chromatin indicate that behavioral changes caused by psychotropic drugs in experimental animals are associated with chromatin alterations and induced macro molecular syntheses; that Parkinsonian and possible drug-induced extrapyramidal symptoms are associated with aberrations in protein synthesis; and that destabilization under the effects of the heterochromatin in schizophrenics seems to be due to histone modifications and is partly prevented by neuroleptic treatment. 53 references. (Author abstract modified)

001556 Stefano, George B.; Kream, Richard M.; Zukin, R. Suzanne. CUNY, Medgar Evers College, Brooklyn, NY 11225 **Demonstration of stereospecific opiate binding in the nervous tissue of the marine mollusc *Mytilus edulis*.** *Brain Research*. 181(2):440-445, 1980.

The presence of stereospecific, high affinity opiate binding sites was demonstrated in neuronal tissue of the invertebrate *Mytilus edulis*, a potentially useful model system for studying the molecular mechanism of opiate action. The binding affinities and sensitivities to salts of the marine mollusc opiate receptor sites were similar to those observed in rat brain. The binding affinity of the opioid peptide (125I)FK33-824 was 10 times greater than that of naloxone. FK33-824 and D-al²-met-enkephalin elevated dopamine levels in *Mytilus edulis* by about 50%. 17 references.

001557 Stein, Donald G.; Blake, Carrie A.; Weiner, Hedy Wald. Dept. of Psychology, Clark University, Worcester, MA 01610 **Nerve growth factor disrupts metabolism and behavioral performance of intact rats but does not affect recovery from hypothalamic lesions.** *Brain Research*. 190(1):278-284, 1980.

Behavioral effects of i.v. nerve growth factor (NGF) to intact, adult rats were investigated, and the consequences of preoperative and postoperative NGF treatments on recovery from deficits that accompany bilateral, simultaneous lesions of the lateral hypothalamic area were studied. Behavioral results indicate that single i.v. injections of NGF into the ventricles can have some effects on discrimination learning long after the treatment has terminated. In addition to the effects of NGF treatments on some aspects of rodent emotionality, consistent and statistically significant increase in variability of performance was observed compared to untreated controls. No evidence was found of sparing or recovery of function when rats with LH lesions were given preoperative long-lasting behavioral and physiological consequences of placing this complex protein into the brain even though it may not be endogenously present in the CNS of the intact animal. 15 references.

001558 Steranka, L. R.; Sanders-Bush, Elaine. Tennessee Neuropsychiatric Institute, Dept. of Pharmacology, Vanderbilt University School of Medicine, Nashville, TN **Long-term effects of**

fenfluramine on central serotonergic mechanisms. *Neuropharmacology*. 18(11):895-903, 1979.

Two weeks after a single injection of 40mg/kg fenfluramine in male Sprague-Dawley rats, brain levels of 5-hydroxytryptamine (5-HT), 5-hydroxyindoleacetic acid (5-HIAA), tryptophan hydroxylase (TPH) activity, and synaptosomal uptake of tritiated 5-HT were markedly reduced. With the exception of TPH activity, these parameters remained significantly decreased for at least 2 months. The largest reductions in 5-HT, 5-HIAA, and 5-HT uptake were found in the hippocampus and cortex, and the largest reductions in TPH activity were found in the midbrain and limbic forebrain. Pretreatment with 10mg/kg fluoxetine prevented the long-term decreases in 5-HT, 5-HIAA, and 5-HT uptake induced by fenfluramine, but did not block the decrease in TPH. Results suggest that the long-term effects of fenfluramine on brain 5-HT neurons cannot be explained by a single mechanism such as an irreversible cytotoxic action. 33 references. (Author abstract modified)

001559 Steranka, Larry R.; Sanders-Bush, Elaine. Dept. of Pharmacology, Tennessee Neuropsychiatric Institute, Nashville, Vanderbilt University School of Medicine, TN **Species differences in the rate of disappearance of fenfluramine and its effects on brain serotonin neurons.** *Biochemical Pharmacology*. 28(20):3103-3107, 1979.

The central serotonergic effects of fenfluramine were compared in male Sprague-Dawley rats and albino mice. A 20mg/kg dose of fenfluramine markedly reduced 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) in rats, but a 80mg/kg dose was required to significantly reduce 5-HT and 5-HIAA in mice. Tryptophan hydroxylase activity was diminished by 60mg/kg fenfluramine in rats, but not by any dose up to 80mg/kg in mice. A 58% reduction in 5-HT uptake was observed after 40mg/kg fenfluramine in rats and 80mg/kg in mice. Mice showed complete recovery within 2 months of fenfluramine administration, when rats reportedly continue to show marked effects. The half-lives of fenfluramine and its active metabolite, norfenfluramine, were much shorter in mice than in rats, which may contribute to the decreased sensitivity of mice to the long-term neurotoxic effects of fenfluramine on central 5-HT systems. 25 references. (Author abstract modified)

001560 Strahlendorf, Howard Kurt. Philadelphia College of Pharmacy and Science **Modification of cortical and subcortical somatosensory evoked potentials by morphine and related compounds.** (Ph.D. dissertation). Dissertation Abstracts International. 40(8):3690-B, 1980. Ann Arbor, Univ. Microfilms No. 8002708, 151p., 1979.

The pharmacodynamics of primary and secondary electrophysiologic responses to opiates were investigated in paralyzed cats under light chloralose anesthesia to elucidate more specifically the effects of narcotic compounds in brain areas participating in reception and integration of nociceptive stimuli. Results indicated that systemically administered morphine exerted a marked, naloxone reversible, enhancement of evoked responses recorded in the centrum medianum of the thalamus and from the primary sensory cortex. Microinjection studies were performed in an attempt to correlate active sites of morphine analgesia with changes in cortical and subcortical evoked potentials. It is suggested that morphine-induced enhancement of somatosensory evoked potentials is mediated in part by cortical, intralaminar thalamic, limbic, and medial diencephalic elements. (Journal abstract modified)

001561 Strahlendorf, J. C.; Strahlendorf, H. K.; Kingsley, R. E.; Gintautas, J.; Barnes, C. D. Dept. of Physiology, Texas Tech University School of Medicine, Lubbock, TX 79430 **Fa-**

cilitation of the lumbar monosynaptic reflexes by locus coeruleus stimulation. *Neuropharmacology*. 19(2):225-230, 1980.

A conditioning train of stimuli delivered in the vicinity of the locus coeruleus elicited a marked facilitation of the lumbar monosynaptic reflex in decerebrated cats. Placement of the electrode in periaqueductal gray resulted in a biphasic facilitatory action in the monosynaptic reflex. Phenoxymethylamine and chlorpromazine caused marked reductions in locus-coeruleus-induced augmentation. Haloperidol appeared to potentiate locus coeruleus elicited facilitation. These data further verify the noradrenergic nature of fibers originating from the locus coeruleus and assign a physiological role to ceruleospinal projection in the regulation of lumbar monosynaptic reflex. 24 references. (Author abstract modified)

001562 Subramanian, N.; Schinzel, W.; Mitznegg, P.; Estler, C.-J. Dept. of Pharmacology, University of Erlangen-Nurnberg, D-8520 Erlangen, Germany **Influence of ethanol on histamine metabolism and release in the rat brain. II. Regions of the histaminergic pathway.** *Pharmacology*. 20(1):42-45, 1980.

The influence of ethanol on histaminergic metabolism and release in the rat brain was investigated. Following acute alcohol administration, histaminic levels of rat brain cortex and thalamus were elevated and histidine decarboxylase activity was decreased. The effect was less pronounced after chronic alcohol treatment. In the striatum there was no change in the metabolic pattern of histamine. Histamine-N-methyltransferase was unaffected in either case. Depolarization-induced release of histamine was inhibited by alcohol in the hypothalamus, thalamus, and cortex. Results indicate that ethanol affects that histamine metabolism and release processes in the histaminergic pathway of the brain. 10 references. (Author abstract modified)

001563 Sugrue, Michael F. Centre de Recherche Merrell International, 16, rue d'Ankara, F-67085 Strasbourg Cedex, France **Changes in rat brain monoamine turnover following chronic antidepressant administration.** *Life Sciences*. 26(6):423-429, 1980.

Changes in rat brain monoamine turnover were studied following the chronic administration of five agents which markedly differ in their patterns of monoamine uptake inhibition. Chronic administration of desipramine or mianserin did not alter turnover of brain dopamine or serotonin. Chronically administered Org 6582, a selective inhibitor of serotonin uptake, decreased basal and attenuated the probenecid-induced increase in brain 5-HIAA levels. Chronically administered desipramine increases rat brain noradrenaline turnover. Acute and chronic Org 6582 administration yield similar findings, a decrease in turnover. It is suggested that rat brain serotonin systems are more resistant than noradrenaline systems to adaptive changes following a prolonged inhibition of monoamine uptake. 44 references. (Author abstract modified)

001564 Supavilai, Porntip; Karobath, Manfred. Karobath: Psychiatrische Universitätsklinik Wien, Lazarettgasse 14, A-1090 Vienna, Austria **Stimulation of benzodiazepine receptor binding by SQ 20009 is chloride-dependent and picrotoxin-sensitive.** *European Journal of Pharmacology*. 60(1):111-113, 1979.

The anxiolytic drugs SQ-20009 and SQ-65396 stimulated the binding of tritiated flunitrazepam to rat brain membranes in a chloride dependent fashion. In the presence of sodium chloride, the stimulation of 3H-flunitrazepam binding by SQ-20009 was consistently higher in cerebellum than in cortex, striatum, or hippocampus. Picrotoxin, which specifically blocks the chloride conductance mechanism associated with the GABA receptor, antagonized the stimulation of 3H-flunitrazepam binding induced by SQ-20009. These findings suggest a functional interaction of benzodiazepine receptors with the chloride conductance

mechanism associated with the GABA/benzodiazepine receptor complex. 4 references.

001565 Suria, Amin. George Washington University School of Medicine, Washington, DC 20037 **Anti-anxiety drugs and cyclic nucleotides.** (Unpublished paper). Final Report, NIMH Grant R03-MH-29771, 1979. 14 p.

To determine the role of cyclic nucleotides and GABA in synaptic activity, the following questions were investigated: 1) if anxiolytics modify synaptic transmission by altering cyclic nucleotides; 2) if anxiolytics alter GABA levels in the ganglion, independent of changes in the nucleotides or as a result of changes in the cyclic nucleotides; and 3) whether the biochemical changes induced by these drugs could be correlated with the electrophysiological events, that is, taking posttitanic potentiation as an index of changes in the presynaptic events. The GABA levels as well as cyclic nucleotides were measured in the superior cervical ganglion (SCG) of rats and frogs. The methodology used is detailed for: estimation of GABA, efflux off 3H-GABA from SCG, estimation of cyclic nucleotides, effect of drugs on GABA levels, effects of drugs on cyclic nucleotide levels, recording of posttitanic potentiation of synaptic potentials from frog sympathetic ganglia, effects of diazepam on GABA content of SCG, cyclic adenosine 3',5'-monophosphate (cAMP) in SCG and effects of diazepam on cAMP, tritiated GABA release from SCG, uptake of 3H-GABA by SCG and effects of various drugs, and effects of decentralization on GABA content of SCG.

001566 Suzuki, Osamu; Hattori, Hideki; Oya, Masakazu; Katsumata, Yoshinao; Matsumoto, Takatoshi. Dept. of Legal Medicine, Hamamatsu University School of Medicine, Hamamatsu 431-31, Japan **Oxidation of beta-phenylethylamine by both types of monoamine oxidase: effects of substrate concentration and pH.** *Life Sciences*. 25(21):1843-1850, 1979.

Beta-phenylethylamine (PEA) was characterized as substrate for both type-A and type-B monoamine oxidase (MAO) in male Sprague-Dawley rat brain mitochondria at different substrate concentrations and with varying pH in the reaction media. Sensitivities to clorgyline and deprenyl indicated that the inhibition patterns with PEA as substrate differed markedly at different substrate concentrations: at 10mM PEA acted as a specific substrate for type-B MAO, but at 50 to 1000mM it became common substrate for both types of MAO. The inhibition patterns were also affected markedly by small changes in pH of the reaction medium: at PEA concentrations of 50 and 100mM, a change in pH from 7.2 to 7.8 resulted in a 20 to 30% increase in the proportion of type-A MAO. Kinetic analyses indicated that the changes in substrate specificity observed at different PEA concentrations and at different pHs may be due to the strong substrate inhibition of type-B MAO. 18 references. (Author abstract modified)

001567 Suzuki, Osamu; Katsumata, Yoshinao; Oya, Masakazu; Matsumoto, Takatoshi. Division of Neurotoxicology, Dept. of Legal Medicine, Nagoya University School of Medicine, Nagoya 466, Japan **Oxidation of phenylethanolamine and octopamine by type A and type B monoamine oxidase.** *Biochemical Pharmacology*. 28(15):2327-2332, 1979.

Phenethanolamine (PEOA) and octopamine (OA) were characterized as substrates for type-A and type-B monoamine oxidase (MAO) by studying sensitivities to the selective MAO inhibitors deprenyl and clorgyline in male Sprague-Dawley rat brain mitochondria. Inhibition patterns with PEOA as substrate differed markedly at different substrate concentrations: at 12.5mM PEOA acted as a specific substrate for type-B MAO, but at 125 and 1250mM it became a common substrate for both

types of MAO. In contrast, OA was found to be a common substrate for both types of MAO at all concentrations tested. Benzyamine was highly specific for type-B MAO over a wide substrate concentration range. 18 references. (Author abstract modified)

001568 Szabadi, E. Dept. of Psychiatry, University of Manchester, Stopford Building, Oxford Road, Manchester M13 9PT, England **Adrenoceptors on central neurones: microelectrophoretic studies.** *Neuropharmacology*. 18(11):831-843, 1979.

A review of the literature concerning neuronal responses to microelectrophoretically applied noradrenaline (NA) suggests that NA has a dual effect on single neurons in many parts of the brain. Studies using specific adrenoceptor agonists and antagonists suggest that excitatory responses to NA are mediated in many cases by alpha-adrenoceptors, while depressant responses are mediated by beta-adrenoceptors. Functionally antagonistic alpha-receptors and beta-receptors may occur on the same neuron. In some structures, the proportions of cells excited or depressed by NA appears to be influenced by factors such as the spontaneous firing rate and the general anesthetic used. These factors may act by altering the relationship between the functionally antagonistic excitatory and inhibitory receptors. 169 references. (Author abstract modified)

001569 Tachizawa, Haruo; Sudo, Kenichi; Sano, Mitsuji. Drug Metabolism Research Center, Research Institute, Daiichi Seiyaku Co., Ltd., 2810 Minamifunabori-cho, Edogawa-ku, Tokyo, 132, Japan **Effect of timiperone on 3H-spiroperidol binding to rat striatal dopamine receptors.** *European Journal of Pharmacology*. 59(3/4):245-251, 1979.

The effects of timiperone, its metabolites, and related compounds on specific 3H-spiroperidol binding to dopamine receptors in male Wistar rat corpus striatum were studied. The receptor affinity of timiperone was about 0.6, 5, and 30 times greater than that of spiroperidol, haloperidol, and chlorpromazine, respectively. Timiperone metabolites showed little or no affinity for the receptors. Results suggest that the potent antipsychotic activity of timiperone is due to the blockade of cerebral dopamine receptors by the unchanged drug. 20 references. (Author abstract modified)

001570 Takano, Shizuko; Sato, Mamoru; Rokkaku, Yuichi; Kaneko, Motohisa; Suzuki, Takehiko. Department of Pharmacology, Fukushima Medical College, Fukushima, 960 Japan **Influence of amoxapine, a new anti-depressant, on platelet aggregation in rabbit.** *Research Communications in Psychology, Psychiatry and Behavior*. 5(1):13-23, 1980.

The influence of amoxapine, imipramine, chlorpromazine, or Li2CO3 on aggregation induced by ADP, noradrenaline combined with 5-HT, or collagen was studied in platelet rich plasma of rabbits. Using rabbit aorta spiral strips, the effect of amoxapine or imipramine on the contraction produced by noradrenaline or 5-HT were examined. On ADP-induced aggregation, none of the drugs showed any influence, with the exception of a disaggregation prompting effect produced by amoxapine. On noradrenaline plus 5-HT-induced aggregation, amoxapine, imipramine, and chlorpromazine showed significant inhibition. On collagen-induced aggregation, amoxapine and imipramine showed significant inhibition. On the contraction produced by noradrenaline in aorta spiral preparation, amoxapine and imipramine showed inhibition of similar degree. On the contraction produced by 5-HT, inhibition of amoxapine was more potent than that of imipramine. 13 references. (Author abstract)

001571 Takano, Yukio; Kohjimoto, Yoshiro; Kamiya, Hiro-O. Dept. of Pharmacology, School of Pharmaceutical Sciences, Fukuoka University, Fukuoka 814, Japan **Effect of psychotropic**

drugs on high affinity choline uptake by excised tissue of rat nucleus caudatus. *Brain Research*. 182(2):478-481, 1980.

The effects of dopaminergic drugs on high affinity choline uptake were determined in tissue removed from the male Wistar rat nucleus caudatus by micropuncture. High affinity choline uptake in the caudate was significantly increased by the dopamine receptor antagonists haloperidol (4mg/kg i.p.) and fluphenazine (5mg/kg i.p.), but significantly decreased by the dopamine receptor agonist apomorphine (10mg/kg i.p.). Results support the existence of inhibitory dopaminergic regulation of striatal cholinergic neurons. 24 references.

001572 Tannenbaum, Gloria Shaffer; Panerai, Alberto E.; Friesen, Henry G. Dept. of Endocrinology, Montreal Children's Hospital, 2300 Tupper Street, Montreal, Quebec H3H 1P3, Canada **Failure of beta-endorphin antiserum, naloxone, and naltrexone to alter physiologic growth hormone and insulin secretion.** *Life Sciences*. 25(23):1983-1990, 1979.

The role of endogenous opiate-like peptides in physiologic regulation of growth hormone (GH) and insulin (IRI) secretion was assessed by passive immunization with beta-endorphin antiserum and by administration of the opiate antagonists naloxone and naltrexone. Six hour secretory profiles were obtained from five groups of freely moving chronically cannulated male rats following the i.v. administration of 1) beta-endorphin antiserum, 2) normal rabbit serum, 3) naloxone (1mg/kg), 4) naltrexone (1mg/kg), and 5) normal saline. The typical ultradian rhythm of GH secretion was evident in all groups with most peak GH values greater than 400mg/ml. No disruption in amplitude or periodicity of the GH rhythm was observed and there was no significant difference in mean 6 hour plasma GH levels. Plasma IRI levels fluctuated minimally over the 6 hr sampling period. There was no significant difference in mean 6 hour IRI levels between groups 1 and 2, or between group 3, 4, and 5. These data do not support the view that endogenous opiate-like peptides play a physiologically important role in maintaining basal GH and IRI secretion. 24 references. (Author abstract)

001573 Taylor, D. A.; Stone, T. W. Dept. of Pharmacology, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver, CO 80262 **The action of adenosine on noradrenergic neuronal inhibition induced by stimulation of locus coeruleus.** *Brain Research*. 183(2):367-376, 1980.

The action of adenosine on noradrenergic neuronal inhibition induced by stimulation of locus coeruleus (LC) was investigated. Stimulation of LC was used to induce a noradrenergic inhibition of neurons on the rat cerebral cortex. The local application of adenosine or adenosine monophosphate by microiontophoresis in the cortex was found to produce a reduction of the evoked inhibition if the purine application was begun 20 seconds before LC stimulation, but an enhancement of the inhibition if applied up to 35 seconds after the LC stimulation. GABA increased the duration of LC inhibition irrespective of time of application. Adenosine and GABA showed no mutual potentiation, but norepinephrine increased the size of responses to both iontophoretic adenosine and GABA. The adenosine/norepinephrine interaction was synergistic, irrespective of the order of application. It is concluded that adenosine may act both presynaptically to inhibit, and postsynaptically to enhance the effects of noradrenergic neurone activation, the dominate effect observed depending on the temporal relationship between LC activation and adenosine application. 32 references. (Author abstract modified)

001574 Tepper, James M.; Schlesinger, Kurt. Dept. of Psychology, University of Colorado, Boulder, CO 80309 **Acoustic prim-**

ing and kanamycin-induced cochlear damage. *Brain Research*. 187(1):81-95, 1980.

The cochleae from three strains of mice, selectively bred for differential susceptibility to priming induced audiogenic seizures, were examined following acoustic priming and retest or kanamycin treatment, and the degree of cochlear damage was assessed. After 60 seconds of acoustic priming, animals from the high and unselected lines which had subsequently developed audiogenic seizure susceptibility exhibited severe cochlear damage limited to the outer hair cells. Low line mice, which had been selected for resistance to acoustic priming-induced audiogenic seizures and were not seizure susceptible, exhibited no cochlear pathology following acoustic priming. Following kanamycin treatment, all three strains developed subsequent audiogenic seizure susceptibility. Histological examination of cochleae from mice so treated revealed a pattern of damage similar to that caused by acoustic priming, except that the cochleae of priming-induced audiogenic seizure resistant low line mice revealed a significant amount of outer hair cell damage. Results are discussed in respect to the physiological mechanisms underlying a selectively bred behavioral phenotype in terms of a possible instance of damage/disuse supersensitivity in the CNS. 29 references. (Author abstract)

001575 Thomas, Thomas N.; Buckholtz, Neil S.; Zemp, John W. Dept. of Biochemistry, Medical University of South Carolina, Charleston, SC 29403 6-Methoxy-1,2,3,4-tetrahydro-beta-carboline effects on retinal serotonin. *Life Sciences*. 25(16):1435-1441, 1979.

The action of 6-methoxy-1,2,3,4-tetrahydro-beta-carboline on the newly identified serotonergic system in bovine retina was studied in vitro. The drug inhibited the high affinity uptake of tritiated 5-hydroxytryptamine (5-HT) in a competitive manner and had no apparent effect on the uptake of dopamine or GABA. The compound also increases the potassium evoked release of 5-HT from the retina. These findings suggest that the retinal 5-HT system may be a site of action for beta-carbolines and similar hallucinogenic drugs. 25 references. (Author abstract modified)

001576 Thompson, Gregory A.; Mudd, S. Harvey; Datko, Anne H.; Giovanelli, John. Laboratory of General and Comparative Biochemistry, NIMH, Bethesda, MD 20205 Regulation of cystathionine gamma-synthase and O-phosphohomoserine sulphydrylase in *Lemma*. (Unpublished paper). Bethesda, MD, NIMH, 1980. 1 p.

Regulation of enzymes of methionine biosynthesis was investigated by measuring activities of O-phosphohomoserine (OPH) dependent cystathionine gamma-synthase and of OPH sulphydrylase in *Lemma paucicostata* growth under various conditions. Activities were determined using modifications of previously described assays. Compounds which block methionine synthesis caused parallel decreases in both activities. DL-propargylglycine caused a 95% reduction in both activities in 18 hours. Sulfate starvation had no effect on either activity. The evidence suggests that: 1) methionine (or a derivative) regulates the amount and/or activity of cystathionine gamma-synthase; and 2) cystathionine gamma-synthase and OPH sulphydrylase may be activities of the same enzyme in *Lemma*. (Author abstract)

001577 Ticku, Maharaj K.; Huang, Ann; Barker, Jeffrey L. Dept. of Pharmacology, University of Texas Health Science Center, San Antonio, TX 78284 GABA receptor binding in cultured mammalian spinal cord neurons. *Brain Research*. 182(1):201-206, 1980.

GABA binding was studied in cell cultures prepared from the spinal cord of 12 to 14 day old C57BL/6J mouse embryos. Re-

sults showed that GABA binds to a single class of binding sites in spinal cord cultured cells; no low affinity binding site comparable to that in mammalian brain was observed. The high affinity site in spinal cord cultures has an affinity similar to that observed in frog spinal cord and to the high affinity site in mammalian brain. It is suggested that cultured spinal cord cells provide a useful model system for analyzing GABA receptor/ionophore function as well as molecular mechanisms of action for benzodiazepines, barbiturates, and convulsant drugs in the GABA synapse. 29 references.

001578 Ticku, Maharaj K.; Olsen, R. W. Olsen: Dept. of Biochemistry, University of California, Riverside, CA 92521 Cage convulsants inhibit picrotoxinin binding. *Neuropharmacology*. 18(3):315-318, 1979.

The effects of bicyclic phosphates and related cage compounds on the binding of tritiated GABA and dihydropicrotoxinin (3H-DHP) to rat brain mitochondrial and microsomal fractions were examined. The cage convulsants did not affect GABA receptor binding, but potentially inhibited the binding of 3H-DHP to membrane sites related to the chloride ion channels regulated by GABA receptors. 10 references. (Author abstract modified)

001579 Traversa, Ugo; Newman, Michael. Institute of Pharmacology, Faculty of Pharmacy, University of Trieste, via A. Valerio 32, I-34100 Trieste, Italy Stereospecific influence of oxazepam hemisuccinate on cyclic AMP accumulation elicited by adenosine in cerebral cortical slices. *Biochemical Pharmacology*. 28(15):2363-2365, 1979.

The effects of enantiomers of the water soluble benzodiazepine oxazepam sodium hemisuccinate on cyclic AMP levels in guinea-pig and Wistar rat cerebral cortex were studied. The accumulation of cyclic AMP elicited by adenosine was decreased by 100mM d-oxazepam sodium hemisuccinate, l-oxazepam sodium hemisuccinate, and d,l-oxazepam sodium hemisuccinate in a manner closely correlated with the drugs' stereostructure and relative anticonvulsant and anxiolytic potencies in vivo. The drugs inhibited uptake of low concentrations of radioactive adenosine into the slices in a similar manner. Addition of theophylline or adenosine deaminase to the superfusion medium sharply decreased both cyclic AMP basal levels and levels elicited by the d-isomer. Results suggest that the interaction of benzodiazepines with their stereospecific receptor sites may be coupled to changes in activity of the adenosine sensitive adenylyl cyclase system and that adenosine may mediate the psychotropic actions of these drugs. 13 references. (Author abstract modified)

001580 Trulson, Michael E.; Jacobs, Barry L. Program in Neuroscience, Dept. of Psychology, Princeton University, Princeton, NJ 08544 Chronic amphetamine administration decreases brain tryptophan hydroxylase activity in cats. *Life Sciences*. 26(5):329-335, 1980.

Chronic administration (6 days) of d-amphetamine sulfate to cats produced significant decreases in the Vmax of brainstem and forebrain tryptophan hydroxylase when measured 1 day and 10 days after the final amphetamine injection. Serotonin and 5-hydroxyindoleacetic acid (5-HIAA) levels were decreased by a similar magnitude. A single injection of amphetamine produced no significant changes in tryptophan hydroxylase activity, serotonin, or 5-HIAA when measured 1 day after the injection. Neither acute nor chronic amphetamine treatment produced any significant changes in the Km of tryptophan hydroxylase for either tryptophan or the natural cofactor, tetrahydrobiopterin. These data suggest that chronic amphetamine treatment decreases central serotonergic neurotransmission by an action on

the rate limiting enzyme in serotonin biosynthesis. 33 references. (Author abstract modified)

001581 U'Prichard, David C.; Enna, S. J. Dept. of Pharmacology, Northwestern University School of Medicine, 303 E. Chicago Avenue, Chicago, IL 60611 **In vitro modulation of CNS beta-receptor number by antidepressants and beta-agonists.** *European Journal of Pharmacology*. 59(3/4):297-301, 1979.

Incubation of rat cerebral cortex slices with antidepressant drugs reduced beta-adrenergic receptor binding of 3H-dihydroalprenolol by 30%. The decrease was maximum after 60 minutes and could be reversed after 120 minutes. A rapid and reversible loss (60%) of beta-receptor binding was also observed after incubation with (-)-isoproterenol, and both effects were due to a decrease in beta-receptor sites. The *in vitro* beta-receptor subsensitivity caused by desipramine and isoproterenol was not additive. 12 references. (Author abstract modified)

001582 U'Prichard, David C.; Reisine, Terry D.; Mason, Stephen T.; Fibiger, Hans C.; Yamamura, Henry I. Dept. of Pharmacology, Northwestern University School of Medicine, Chicago, IL 60611 **Modulation of rat brain alpha- and beta-adrenergic receptor populations by lesion of the dorsal noradrenergic bundle.** *Brain Research*. 187(1):143-154, 1980.

The modulation of rat brain alpha-adrenergic and beta-adrenergic receptor populations by lesion of the dorsal noradrenergic bundle was investigated. Bilateral lesion of the ascending noradrenergic fibers in the dorsal bundle of adult Wistar rats with 4mcg of 6-hydroxydopamine caused extensive depletion of norepinephrine in all forebrain areas, but led to a 54% increase in norepinephrine levels in the cerebellum. Beta-adrenergic receptor binding of (3H)dihydroalprenolol was significantly increased in all forebrain areas depleted of norepinephrine except the hypothalamus. The increase in (3H)dihydroalprenolol binding was due to 62% and 34% increases in the number of beta-receptor sites in the frontal cerebral cortex and hippocampus respectively. Binding of (3H)WB-4101 to alpha-adrenergic receptors after dorsal bundle lesion was augmented generally to a lesser extent than beta receptor binding, with significantly increased numbers of sites only in the frontal cortex (74%), thalamus (20%), and septum. Both alpha and beta receptor binding sites were reduced in number by 25% to 28% in the cerebellum of dorsal bundle lesioned rats, whereas intraventricular administration of 6-hydroxydopamine to adult rats, which depletes norepinephrine in the cerebellum by 96% increased cerebellar alpha and beta receptor binding by 33% to 40%. Binding of (3H)clonidine to forebrain alpha2 adrenergic receptors was significantly elevated in the frontal cortex, but reduced in the amygdala and septum, after dorsal bundle lesion. 35 references. (Author abstract modified)

001583 Vacca, Linda L.; Abrahams, Susan J.; Naftchi, N. Eric. Dept. of Pathology, Medical College of Georgia, Augusta, GA **Effect of morphine on substance P neurons in rat spinal cord: a preliminary study.** *Brain Research*. 182(1):229-236, 1980.

A study of the effects of morphine on substance-P immunoreactivity in the spinal cord of female Wistar rats is described. Preliminary findings indicate that chronic administration of moderate doses of morphine sulfate increases the level of immunoreactive substance-P in the substantia gelatinosa and in certain other regions of the spinal cord. The increased amount of substance-P in the dorsal horn is correlated with the distribution of opiate receptors, and the increased substance-P in processes of the ventral horn suggests a relationship with nociception, analgesia, and motor function. 39 references.

001584 van Houten, Mark; Posner, Barry I. Department of Medicine, McGill University, Montreal, Quebec, H3A 2B2,

Canada Insulin binds to brain blood vessels *in vivo*. *Nature*. 282(5739):623-625, 1979.

An attempt to localize rat cell types possessing insulin receptors morphologically using light and electron microscope autoradiography is reported. 125I labelled porcine insulin in the absence or coexistent presence of graduated amounts of unlabelled insulin, or structurally dissimilar polypeptides, ovine prolactin or bovine adrenocorticotrophic hormone (ACTH), was injected intracardially into anesthetized male rats. Results indicate that blood vessels throughout the CNS of the rat bind plasma insulin rapidly and with considerable specificity. All regions of the brain examined were found to show vascular binding of insulin, although there was considerable regional variation in insulin binding capacity. It is suggested that insulin may exert a generalized effect on brain activity by a direct action on aspects of blood-brain barrier function perhaps unrelated to glucose uptake. 12 references. (Author abstract modified)

001585 Vern, Boris A.; Schuette, William H.; Mutsuga, Naomi; Whitehouse, Willard C. Clinical Neurosciences Branch, National Institute of Neurological and Communicative Disorders and Stroke, NIH, Bethesda, MD 20014 **Effects of ischemia on the removal of extracellular potassium in cat cortex during pentylenetetrazol seizures.** *Epilepsia*. 20(6):711-724, 1979.

Changes in cortical extracellular potassium activity, NADH fluorescence, and oxygen consumption were studied in anesthetized cats during pentylenetetrazol seizures. The effects of partial ischemia induced by either hypotension or intermittent carotid artery occlusion on these parameters were investigated. Nonischemic seizures were characterized by gradual generalized decreases in cortical NADH fluorescence and increases in oxygen consumption, along with rapid increases in potassium, which then usually fell slightly as the ictal discharge continued. Ischemic seizures, on the other hand, were accompanied by complex changes in NADH fluorescence, by smaller delayed maximal increases in oxygen consumption that lasted beyond the end of ictal activity, and by more sustained increases in potassium. Results suggest that an oxygen dependent transport mechanism plays a major role in the removal of potassium during and after generalized pentylenetetrazol seizures in the cat. 32 references. (Author abstract modified)

001586 Versteeg, Dirk H. G.; De Kloet, E. Ronald; De Wied, David. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Utrecht, The Netherlands **Effects of alpha-endorphin, beta-endorphin and (des-tyr1)-gamma-endorphin on alpha-MPT-induced catecholamine disappearance in discrete regions of the rat brain.** *Brain Research*. 179(1):85-92, 1979.

Intracerebroventricular administration of 100ng alpha-endorphin, beta-endorphin, or (des-tyrosine1)-gamma-endorphin altered the alpha-methyl-p-tyrosine-induced disappearance of catecholamines from discrete regions of the male Wistar rat brain. Alpha-endorphin decreased the disappearance of noradrenaline (NA) in the medial septal nucleus, dorsomedial nucleus, central amygdaloid nucleus, subiculum, ventral part of the nucleus reticularis medullae oblongatae, and the A1 region; dopamine (DA) disappearance was decreased in the caudate nucleus, globus pallidus, medial septal nucleus, nucleus interstitialis striae terminalis, paraventricular nucleus, zona incerta, and central amygdaloid nucleus. Beta-endorphin decreased NA disappearance from the ventral part of the nucleus reticularis medullae oblongatae, DA disappearance from the lateral septal nucleus, and the disappearance of both amines from the rostral part of the nucleus tractus solitarius; DA disappearance was increased in the medial septal nucleus and zona incerta. Following (des-tyrosine1)-gamma-endorphin, NA disappearance was enhanced in the an-

terior hypothalamic nucleus and DA disappearance was increased in the paraventricular nucleus, zona incerta, and rostral part of the nucleus tractus solitarius; NA disappearance was decreased in the periventricular thalamus and the A7 region. 25 references. (Author abstract modified)

001587 Vincent, Steven R.; McGeer, Edith G. Kinsmen Laboratory of Neurological Research, Dept. of Psychiatry, University of British Columbia, Vancouver, BC V6T 1W5, Canada **A comparison of sodium-dependent glutamate binding with high-affinity glutamate uptake in rat striatum.** *Brain Research.* 184(1):99-108, 1980.

The specific sodium dependent binding of (3H)glutamate to membranes of the rat striatum was examined and a comparison made with high affinity glutamate uptake. In the presence of sodium, (3H)glutamate binding was saturable and of high affinity. No binding could be detected in the absence of sodium. Removal of the cortical afferents to the striatum resulted in a parallel decrease in Na dependent glutamate binding and in high affinity glutamate uptake. Drugs which inhibit high affinity uptake were also effective at inhibiting Na dependent binding. It is suggested that about half the Na dependent glutamate binding sites in the striatum represent high affinity uptake sites on the corticostriatal terminals; the remainder of the binding sites are located on striatal neurons and may also be uptake sites. 36 references. (Author abstract modified)

001588 Waddingham, Stephanie Frances Taylor. University of Texas at Austin **Pharmacogenetic analysis of sedative-hypnotic drug dependence: the role of adrenergic and gabaminergic neurotransmission.** (Ph.D. dissertation). Dissertation Abstracts International. 39(7):3578-B, 1979. Ann Arbor, Univ. Microfilms No. 7900661, 123p., 1977.

Several compounds known to possess highly specific receptor blocking actions were screened for reduction of phenobarbital withdrawal severity in two strains of inbred mice. Phenoxybenzamine, propranolol and haloperidol significantly reduced the frequency of barbiturate withdrawal seizures in C57BL/6J mice. The course of withdrawal in DBA/2J mice was unaffected by any adrenergic receptor antagonist. Aminoxyacetic acid had no effect on withdrawal in either strain. It is suggested that there appears to be some degree of genetic determination in the density of the receptor in the central nervous system of these inbred mice. (Journal abstract modified)

001589 Waddington, J. L.; Cross, A. J.; Longden, A.; Owen, F.; Poulter, M. Division of Psychiatry, MRC Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ, England **Functional distinction between DA-stimulated adenylate cyclase and 3H-spiroperone binding sites in rat striatum.** *European Journal of Pharmacology.* 58(3):341-342, 1979.

Striatal dopamine (DA) stimulated adenylate cyclase (AC) activity and 3H-spiroperone binding were correlated with apomorphine induced rotational behavior in male Sprague-Dawley rats with unilateral 6-hydroxydopamine lesions of the medial forebrain bundle. A significant positive correlation was found between rotational responses to apomorphine and 3H-spiroperone binding, but a weak negative correlation was found between rotation and AC activity. These findings suggest a functional distinction between the AC linked DA-1 receptor and DA-2 receptors, which are able to bind butyrophenone neuroleptics and are not linked to AC. 5 references.

001590 Wade, Patricia D.; Timiras, Paola S. Dept. of Cell Biology, Rockefeller University, 1230 York Avenue, New York, NY 10021 **Whole brain and regional (125I)-alpha-bungarotoxin binding in developing rat.** *Brain Research.* 181(2):381-389, 1980.

The specific binding of (125I)-alpha-bungarotoxin (125I-a-BGT), which labels nicotinic acetylcholine receptors, was studied in the developing rat brain. In most brain regions, 125I-a-BGT specific binding was measurable but low on postnatal day 1, peaked at 12 to 20 days of age, and declined by adulthood. With a few exceptions, these data held true for binding expressed as specific binding/mg protein, specific binding/gram wet tissue, or total specific binding/brain region. Whole brain showed the same age related pattern as most of the brain regions, with fewer total binding sites in adult brain than at 19 to 20 days of age. 27 references. (Author abstract modified)

001591 Wahlstrom, Goran. Dept. of Pharmacology, University of Umea, S-901 87 Umea, Sweden **The interaction between atropine and the steric isomers of hexobarbital in normal rats and rats made tolerant to barbitol.** *European Journal of Pharmacology.* 59(3/4):219-225, 1979.

The effects of pretreatment with atropine on the hexobarbital anesthesia threshold in normal and barbitol tolerant male Sprague-Dawley rats were determined, using racemic hexobarbital or its stereoisomers. Atropine reduced the threshold when tested with racemic hexobarbital in normal rats. Atropine significantly reduced the threshold for (S)-hexobarbital but not for (R)-hexobarbital, suggesting that specific cholinergic activity may be involved only in the effect of the (S)-isomer. Tolerance to hexobarbital was seen in barbitol tolerant animals tested with racemic hexobarbital or the (R)-isomer, but only a slight increase in threshold was seen in the test with the (S)-isomer, but only when tested with the racemate or R-isomer; a nonsignificant increase was seen with the (S)-isomer. Results suggest that the excitation measured as tolerance after long-term barbitol treatment may be due to cholinergic hyperactivity. 30 references. (Author abstract modified)

001592 Waldmeier, P. C.; Maitre, L. Research Dept., Pharmaceuticals Division, CIBA-GEIGY Ltd., Basel, Switzerland **The use of scopolamine for the estimation of the central antiacetylcholine properties of neuroleptics.** *Journal of Pharmacy and Pharmacology.* 31(8):553-555, 1979.

An attempt was made to quantify the antagonistic effect of a maximally active dose of scopolamine on the increase in tyrosine hydroxylation in vivo elicited by a series of neuroleptic agents of different intrinsic antimuscarinic potency. All the drugs used caused a dose related increase in tyrosine hydroxylation in both the striatum and the mesolimbic area. The effect of haloperidol and to a lesser extent, that of clozapine and chlorpromazine, was clearly more pronounced in the striatum than in the mesolimbic area. This difference was less obvious in the tissues of animals treated with thioridazine, sulpiride, and GP 50302. All the dose response curves were shifted to the right by scopolamine, but to a varying extent. It is concluded that the increase in dopamine (DA) turnover produced by neuroleptics with little or no intrinsic antiacetylcholine (AntiACh) effect is readily antagonized by high doses of scopolamine, while the effect of strongly AntiACh neuroleptics (clozapine and thioridazine) are only weakly antagonized. 21 references.

001593 Walters, J. R.; Lakoski, J. M.; Baring, M. D.; Eng, N. NIH, 9000 Rockville Pike, Bldg. 36, Rm. 5A31, Bethesda, MD 20205 **Dopamine neurons: effect of lergotril on unit activity and transmitter synthesis.** *European Journal of Pharmacology.* 60(2/3):199-210, 1979.

Lergotril mesylate caused a rapid, dose dependent, and haloperidol reversible inhibition of unit activity of dopamine (DA) cells in the pars compacta of the male Sprague-Dawley rat substantia nigra. A 6mcg/kg dose caused significant depression of DA cell firing rates, and a cumulative dose of 100mcg/kg dose

caused 50% inhibition. Pretreatment with reserpine and alpha-methyl-p-tyrosine did not significantly attenuate the lergotril-induced inhibition. Lergotril had no consistent effect on firing rates of cells in the pars reticulata. Lergotril reduced the activation of striatal DA synthesis associated with the complete cessation of impulse flow in nigrostriatal DA neurons following gamma-butyrolactone treatment. Results suggest that lergotril is a direct acting DA agonist. 40 references. (Author abstract modified)

001594 Walton, Kenneth G.; Miller, Edith; Baldessarini, Ross J. Laboratories of Psychiatric Research, Mailman Research Center, McLean Hospital, Belmont, MA 02178 **Prenatal and early postnatal beta-adrenergic receptor-mediated increase of cyclic AMP in slices of rat brain.** *Brain Research*. 177(3):515-522, 1979.

Levels of cyclic AMP in slices of cerebral cortex and cerebellum from newborn Sprague-Dawley rats were significantly but transiently increased by exposure to the beta-adrenergic agonist isoproterenol. Isobutylmethylxanthine, an inhibitor of phosphodiesterase, enhanced this effect and permitted its detection in cerebral cortex obtained from prenatal rats. Results are consistent with the view that functional adrenergic synapses are formed early in the ontogeny of the CNS and that norepinephrine exerts cyclic AMP mediated influences on brain development. 50 references. (Author abstract modified)

001595 Wamsley, James K.; Black, Asa C., Jr.; West, James R.; Williams, Terence H. Dept. of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, 725 North Wolfe St., Baltimore, MD 21205 **Cyclic AMP synthesis in guinea pig superior cervical ganglia: response to pharmacological and preganglionic physiological stimulation.** *Brain Research*. 182(2):415-421, 1980.

Cyclic AMP levels in guinea-pig superior cervical ganglia (SCG) incubated in Eagle's medium with 5mM theophylline were not altered by the addition of 50mM dopamine, but were doubled by the addition of 50mM norepinephrine and increased sixfold by 50mM isoproterenol. The increases were blocked by propranolol, indicating they were due to stimulation of a beta-adrenergic receptor/adenylate cyclase complex. In contrast, in rabbit SCG, dopamine increased cyclic AMP levels to 60% above control values. When the SCG were subjected to supramaximal stimulation for 8 minutes, cyclic AMP levels were doubled in the rabbit SCG but were not altered in the guinea-pig SCG. Results suggest that the modulation of neural transmission in the guinea-pig SCG does not involve a dopamine receptor/adenylate cyclase complex. 25 references. (Author abstract modified)

001596 Wang, R. Y.; de Montigny, C.; Gold, B. I.; Roth, R. H.; Aghajanian, G. K. Dept. of Pharmacology, St. Louis University School of Medicine, 1402 S. Grand Blvd., St. Louis, MO 63104 **Denervation supersensitivity to serotonin in rat forebrain: single cell studies.** *Brain Research*. 178(2-3):479-497, 1979.

The development of denervation supersensitivity to 5-hydroxytryptamine (5-HT) in the amygdala (AMYG) and ventral lateral geniculate nucleus (vLGN) was studied in Sprague-Dawley rats. Following destruction of 5-HT projections to the vLGN and AMYG with 5,7-dihydroxytryptamine (5,7-DHT), enhanced responsiveness of cells to the inhibitory effect of microiontophoretically applied 5-HT was apparent within 24 hours, with a maximum effect 7 days after the 5,7 DHT treatment. In general, the time course for the reduction in the density of 5-HT fluorescent varicosities and synaptosomal 5-HT uptake activity paralleled the time course for the development of denervation supersensitivity to 5-HT. The enhanced sensitivity

was initially selective for 5-HT, but increased responsiveness to norepinephrine, GABA, and lysergic acid diethylamide was also observed 7 or more days after 5,7-DHT. Chronic administration of parachlorophenylalanine, a 5-HT synthesis inhibitor, failed to induce 5-HT supersensitivity. 68 references. (Author abstract modified)

001597 Warbritton, John D., III; Stewart, R. Malcolm; Baldessarini, Ross J. Baldessarini: Mailman Research Center, McLean Hospital, 115 Mill Street, Belmont, MA 02178 **Increased sensitivity to intracerebroventricular infusion of serotonin and deaminated indoles after lesioning rat with dihydroxytryptamine.** *Brain Research*. 183(2):355-366, 1980.

The increased sensitivity to intracerebroventricular infusion of serotonin (5-HT) and deaminated indoles after lesioning rat with 5,7-dihydroxytryptamine (DHT) was investigated. Intracerebroventricular infusion of a placebo or 5-hydroxyindoleacetic acid (t-HIAA) had little effect, but 5-HT decreased, and norepinephrine increased, locomotor activity in intact rats. Following pretreatment with 5,7-DHT, a small increase in locomotor activity was noted which was not altered by intracranial infusion of vehicle. In contrast, infusions of 5-HT produced a striking dose dependent pattern of hyperactivity, myoclonic jerking movements, postural changes, and autonomic responses. Norepinephrine increased locomotor activity in the DHT lesioned rats (but not significantly more than in controls), but failed to produce the myoclonic syndrome. The deaminated indoles, indoleacetaldehyde and 5-HIAA were more potent than 5-HT in producing the myoclonic response; tryptamine when infused at an equimolar dose had no effect. The putative serotonin antagonists, cyproheptadine and methiothepin (i.p.), were more effective in blocking responses to infused 5-HT than to equipotent doses of deaminated indoles. These behavioral responses may represent exaggerated excitatory effects mediated by serotonin in the brainstem and spinal cord, possibly modified by altered fore-brain mechanism. 55 references. (Author abstract modified)

001598 Wasterlain, C. G.; Jonec, V. Epilepsy Research Laboratory, V.A. Medical Center, Sepulveda, CA 91343 **Muscarinic kindling: transsynaptic generation of a chronic seizure focus.** *Life Sciences*. 26(5):387-391, 1980.

Daily injections of subconvulsive amounts of carbamylcholine or muscarine into the L-basolateral amygdala of Holzman rats resulted in the progressive development of kindled seizures. Addition of equimolar atropine to carbachol completely prevented development of seizures. Rats kindled with carbachol had full seizures when tested for the first time with muscarine and vice versa. Kindling persisted after 4 weeks without stimulation and spontaneous seizures were observed. No histological differences existed between carbachol kindled and carbachol atropine (non-kindled) rats. These data suggest that a chronic epileptic focus was induced transsynaptically. 12 references. (Author abstract)

001599 Watkins, J. C. Dept. of Physiology, The Medical School, Bristol BS8 1TD, England **NMDA receptors: new light on amino acid-mediated synaptic excitation.** *Trends in Neurosciences*. 3(3):61-64, 1980.

The recent research literature on N-methyl-D-aspartic acid (NMDA) receptors, which are closely associated with spinal synaptic excitation, is discussed. It is noted that the investigation of the role of amino acids as excitatory synaptic transmitters has progressed rapidly since the discovery of a range of specific antagonists. NMDA receptors are very sensitive to the concentration of magnesium ions in the extracellular fluid, and may be activated by a synaptically released neurotransmitter. Topics discussed include: glutamate and aspartate analogues, different glutamate and aspartate receptors, screening techniques, transmitter

identification, and implications for pharmacotherapy in mental illness. 7 references. (Author abstract modified)

001600 Wattiaux, R.; Wattiaux-De Coninck, S. Laboratoire de Chimie Physiologique, Facultés Universitaires Notre-Dame de la Paix, 61, rue de Bruxelles, Namur, Belgium **Reversible and irreversible alterations of lysosomes in ischemic rat-liver: effects of chlorpromazine.** *Biochemical Pharmacology*. 29(6):963-966, 1980.

The fate of two lysosomal hydrolases, acid phosphatase and beta-galactosidase, was investigated in rat liver lobes immediately after an ischemic period of 20 hours after reestablishment of the circulation. Some of the rats were pretreated with chlorpromazine. The free activity of acid phosphatase was increased twofold in the homogenates of livers deprived of blood for 1 hour. Twenty hours after the return of blood flow, a quasi normal free activity was recovered. The change of unsedimentable beta-galactosidase paralleled that of free acid phosphatase. Thus, 1 hour ischemia caused a lysosomal lesion which was reversible to a large extent. When the blood supply was cut off for 2 hours, the increase of the free and soluble activities of acid hydrolases was more impressive, and reestablishment of the circulation did not lead to recovery. Pretreatment with chlorpromazine opposed the irreversible effect of ischemia on the lysosomal hydrolase latency. Thus, it is concluded that a lysosomal lesion may be reversible and that this reversibility may be favorably influenced with the help of a drug. 7 references.

001601 Wecker, Lynn; Schmidt, Dennis E. Dept. of Pharmacology, Louisiana State University Medical Center, 1542 Tulane Avenue, New Orleans, LA 70112 **Neuropharmacological consequences of choline administration.** *Brain Research*. 184(1):234-238, 1980.

The effects of choline pretreatment on dose-dependent atropine-induced acetylcholine (ACh) depletion in rat striatum and hippocampus were examined. Acute administration of choline iodide to rats caused a significant increase in the concentration of free choline in brain 15 minutes after injection. Maximal effects were noted following the administration of 60mg/kg and choline levels increased to 132% and 151% of controls in the caudate-putamen and hippocampus, respectively. Levels returned to control by 30 minutes and remained constant thereafter. It is concluded that evidence supports the hypothesis that choline availability is a significant factor determining the responsiveness of central cholinergic neurons to pharmacological manipulation. 13 references.

001602 Weinberger, Jesse; Greenberg, Joel H.; Waldman, Maria T. G.; Sylvestro, Angelina; Reivich, Martin. Dept. of Neurology, Mount Sinai School of Medicine, New York, NY 10029 **The effect of scopolamine on local glucose metabolism in rat brain.** *Brain Research*. 177(2):337-345, 1979.

The effects of the muscarinic acetylcholine inhibitor scopolamine (0.4mg/kg i.v.) on local cerebral glucose metabolism (LCMRG) was examined in male Wistar rats, using the [¹⁴C]-2-deoxyglucose autoradiographic technique. The greatest decrease in LCMRG occurred in the globus pallidus (to 57.5% of control value). LCMRG in the caudate nucleus was decreased to 82.6%, in Ammons horn of hippocampus to 61.6%, and in the dentate gyrus to 71.8%. The auditory (67.3%), frontal (70.7%), and parietal (70.1%) cortices and the lateral thalamus (73.1%) were all significantly depressed. Changes in limbic structures, including the hypothalamus (75.0%), mammillary body (75.1%), septal nuclei (80.5%), and nucleus accumbens (89.0%) were not as marked. Brainstem and cerebellar structures were not significantly affected. The involvement of cholinergic pathways in which scopolamine reduced LCMRG in the drug's effects on memory is discussed. 24 references. (Author abstract modified)

001603 Weinstock, Marta; Zavadil, Anthony P., III; Kopin, Irwin J. Kopin: Laboratory of Clinical Science, NIMH, Building 10, Room 2D-46, Bethesda, MD 20205 **Differential effects of d- and l-propranolol on dopamine turnover stimulated by oxotremorine in striatal and mesolimbic areas of rat brain.** *European Journal of Pharmacology*. 59(3/4):187-193, 1979.

The effects of l-propranolol, d-propranolol, and clonidine on homovanillic acid (HVA) concentrations in the male Sprague-Dawley rat corpus striatum and nucleus accumbens were studied under normal conditions and after treatment with oxotremorine or haloperidol. Propranolol and clonidine had no significant effect on HVA levels in either area when given alone, but l-propranolol (1 to 10mg/kg) and clonidine (0.1mg/kg) both significantly inhibited the elevation of striatal HVA after oxotremorine. Both isomers of propranolol reduced the effect of oxotremorine in the nucleus accumbens. The rise in HVA induced by haloperidol was not altered by l-propranolol or clonidine. Results suggest that propranolol may reduce cholinergic activation of dopaminergic pathways by two mechanisms; one is stereospecific for the l-isomer and operates in the striatum, while the second is shared by both isomers in the nucleus accumbens. 32 references. (Author abstract modified)

001604 Whall, Clifford W., Jr.; Myers, Michael M.; Halpern, William. Dept. of Physiology, 7710 Medical Science II, University of Michigan, Ann Arbor, MI 48109 **Norepinephrine sensitivity, tension development and neuronal uptake in resistance arteries from spontaneously hypertensive and normotensive rats.** *Blood Vessels*. 188:1-19, 1979.

Intact segments of mesenteric resistance arteries from 5-month-old spontaneously hypertensive (SHR) and normotensive Wistar Kyoto (WKY) rats were tested for norepinephrine (NE) sensitivity: dose response curves were obtained both before and after adrenergic denervation produced by short-term, in vitro, 6-hydroxydopamine (6-OHDA) treatment. NE sensitivities of innervated vessels were the same in SHR and WKY rats; however, after 6-OHDA, not only did both ED50s show significant decreases, but the ED50 of SHR vessels was half that of WKY (NE sensitivity increased twofold). In addition, there was a 33% increase in wall tension generated in response to maximum NE stimulation, and a 44% increase in neuronal NE uptake in the SHR vessels. Thus, the mesenteric resistance arteries from the SHR rats showed an increase in two parameters intrinsic to the smooth muscle, namely vascular smooth muscle sensitivity to NE and developed NE wall tension, and one extrinsic parameter, rate of neuronal uptake, when compared to WKY controls. One or both of the intrinsic factors could account in part for the observed increases in total peripheral resistance and vascular reactivity characteristically seen in perfused beds from the SHR rats 40 references. (Author abstract modified)

001605 Wheal, H. V.; Miller, J. J. Neurophysiology Group, University of Southampton, Southampton, England **Pharmacological identification of acetylcholine and glutamate excitatory systems in the dentate gyrus of the rat.** *Brain Research*. 182(1):145-155, 1980.

Stimulation of the medial septum and perforant path of urethane anesthetized Wistar rats evoked an orthodromic activation of dentate granule cells associated with the negative transient of the characteristic field potential elicited from each site. The excitatory action of acetylcholine (ACh) on these cells was antagonized by atropine, but the excitatory effects of glutamate (Glu) were not. Glutamate diethylester (GDEE) blocked the excitation produced by Glu but not ACh. The synaptically evoked excitation elicited by medial septal stimulation was blocked by atropine but unaltered by GDEE, whereas the perforant path excitatory response was blocked by GDEE and unaltered by at-

ropine. Results indicate that two discrete excitatory systems are present in the dentate gyrus of the rat, a cholinergic system originating in the medial septum and a glutamate mediated system originating in the entorhinal cortex. 35 references. (Author abstract modified)

001606 White, W. F.; Nadler, J. V.; Cotman, C. W. Cotman: Dept. of Psychobiology, University of California, Irvine, CA 92717 **Analysis of short-term plasticity at the perforant path-granule cell synapse.** *Brain Research.* 178(1):41-53, 1979.

Short-term plasticity was investigated at the perforant path/granule cell synapse in the rat hippocampal slice preparation. Habituation and paired pulse potentiation were both demonstrated at the perforant path/granule cell synapse, and the magnitude of both forms of plasticity was inversely related to the amplitude of the initial extracellular excitatory postsynaptic potential. Studies with the reversible antagonist 2-amino-4-phosphonobutyric acid indicated that both forms of plasticity resulted from presynaptic changes, presumably involving modulation of transmitter release. 20 references. (Author abstract modified)

001607 White, W. F.; Snodgrass, S. R.; Dichter, M. Dichter: Dept. of Neurology Harvard Medical School, Boston, MA 02115 **Identification of GABA neurons in rat cortical cultures by GABA uptake autoradiography.** *Brain Research.* 190(1):139-152, 1980.

Autoradiographic studies of rat cortical cultures were conducted with tritiated transmitters and related drugs. Autoradiographs prepared from cultures incubated in (3H)GABA showed selective labeling. Results suggest a metabolic, rather than a neurotransmitter, role for glycine in the cultures, as would be expected of neuronal cells derived from cerebral cortex. Results also demonstrate that the affinity of muscimol for the GABA uptake site far outweighs its affinity for the GABA receptor site in autoradiographic experiments where intact cells are employed, presumably because its binding to receptors is fleeting. These autoradiographic studies suggest that nearly half the neurons in the culture system are GABA neurons but disclosed no morphological handle for GABA neurons. 48 references. (Author abstract modified)

001608 Wiernsperger, Nicolas; Gyga, Peter; Schweizer, Alfred; Danzeisen, Max. Pharmaceutical Division, Preclinical Research, Sandoz Ltd., Basel, Switzerland **Dopaminergic agonists and their influence on the oxygenation and functional activity of underperfused brain tissue.** *European Journal of Pharmacology.* 60(2/3):115-119, 1979.

The effects of apomorphine and bromocriptine on brain electrical activity and oxygen supply were studied in cats subjected to hypovolemic oligemia. Both dopaminergic agonists stimulated the brain by prolonging the oligemia-induced seizures in the caudate nucleus and in the cerebral cortex, but only apomorphine improved the pO₂ distribution in the cortical tissue after 120 minute oligemia. Bromocriptine had a beneficial effect of shorter duration. Results indicate that the brain can be activated even under conditions of incomplete ischemia. The differential effects of the two drugs support the hypothesis that at least two types of dopamine receptors exist in brain. 17 references. (Author abstract modified)

001609 Wigston, D. J. Dept. of Physiology and Biophysics, Washington University School of Medicine, 660 South Euclid Ave, St Louis, MO 63110 **Transmitter release from nerve terminals undergoing suppression.** *Brain Research.* 190(1):175-183, 1980.

The mechanism behind the decline in quantal content of foreign nerve transmission in the axolotl supracoracoideus muscle

was investigated. The effect of K on spontaneous transmitter release from suppressed foreign terminals was investigated after the degeneration of native terminals. All terminals studied responded with an increase in spontaneous miniature endplate potential frequency. Transmitter release from suppressed terminals was compared with that from nonsuppressed terminals. The possibility that the lower level of spontaneous and evoked transmitter release from suppressed terminals may be due to a reduced overall number of Ca²⁺ channels in the terminal membrane or a reduced availability of transmitter release sites is compatible with a reduction in the site of the nerve terminal during suppression. 17 references. (Author abstract modified)

001610 Wilkening, D.; Dvorkin, B.; Makman, M. H.; Lew, J. Y.; Matsumoto, J.; Baba, Y.; Goldstein, M.; Fuxe, K. Dept. of Molecular Pharmacology, Albert Einstein College of **Catecholamine-stimulated cyclic AMP formation in phenylethanolamine N-methyltransferase containing brainstem nuclei of normal rats and of rats with spontaneous genetic hypertension.** *Brain Research.* 186(1):133-143, 1980.

Stimulation of cyclic AMP formation by epinephrine and norepinephrine was studied in discrete areas of rat brain that include the epinephrine containing brainstem nuclei C-1 and C-2. In the C-1 area, epinephrine stimulated cyclic AMP formation was partially reversed by 100μM phentolamine and 10 to 100μM propranolol or alprenolol and hence appeared to involve activation of a mixture of both alpha and beta-adrenergic receptors. However, in the C-2 area, the epinephrine and norepinephrine stimulated cyclic AMP formation involved the activation of a single receptor type which was alpha-like in character. Stimulation of cyclic AMP formation by epinephrine in the C-2 area was antagonized by nanomolar concentrations of both phentolamine and yohimbine. The epinephrine stimulated formation of cyclic AMP in the C-2 but not in the C-1 area was augmented in a strain of rats which exhibited spontaneous genetic hypertension (SHR) vs. Wistar-Kyoto controls. It is suggested that this enhanced formation could be a physiological compensatory response to some other hypertension causing lesion which leads to postsynaptic receptor supersensitivity. Supporting this possibility was the finding that reserpine essentially obliterated the difference between control and SHR rats. The findings are also interpreted as supporting the involvement of epinephrine neurons in central vasodepressor mechanisms. 29 references. (Author abstract modified)

001611 Wilkening, Douglas; Sabol, Steven L.; Nirenberg, Marshall. Laboratory of Biochemical Genetics, NHLBI, Bethesda, MD 20205 **Control of opiate receptor-adenylate cyclase interactions by calcium ions and guanosine-5'-triphosphate.** *Brain Research.* 189(2):459-466, 1980.

The effect of morphine on adenylate cyclase and the extent of inhibition of adenylate cyclase by morphine or norepinephrine as a function of Ca²⁺ ion concentrations were studied. Adenylate cyclase of homogenates of NG108-15 neuroblastoma by glioma hybrid cells is activated by low concentrations of Ca²⁺ ions and is inhibited by higher (greater than 0.1 mM) concentrations of Ca²⁺ ions. Activation of either opiate receptors by 10mM morphine or alpha-adrenergic receptors by 10mM norepinephrine inhibits adenylate cyclase by 55% in the absence of Ca²⁺ ions, and inhibits the Ca²⁺ dependent activation of adenylate cyclase by more than 90%. Concentrations of Ca²⁺ ions greater than 0.1 mM inhibit adenylate cyclase and also reduce the extent inhibition of adenylate cyclase by morphine but not by norepinephrine. Guanosine-5'-triphosphate is required for inhibition of adenylate cyclase or morphine. Results show that morphine inhibits adenylate cyclase by a guanosine-5'-triphosphate dependent process and that the extent of inhibition of adenylate cyclase by morphine or norepinephrine is a function of the Ca²⁺ ion concentra-

tion and the proportion of adenylate cyclase molecules that are activated or inhibited by Ca^{2+} ions. 25 references. (Author abstract modified)

001612 Williford, D. J.; DiMicco, J. A.; Gillis, R. A. Dept. of Pharmacology, Georgetown University School of Medicine, Washington, DC 20007 **Evidence for the presence of a tonically active forebrain GABA system influencing central sympathetic outflow in the cat.** *Neuropharmacology*. 19(3):245-250, 1980.

The central sympathetic effects of bicuculline in the cat were investigated to determine if they are localized in forebrain areas. Administration of 1, 5, and 27mcg doses into the lateral and third ventricles caused dose dependent increases in arterial pressure and heart rate (HR) while the same doses administered into the fourth ventricle had no significant effect on HR and only a slight effect on pressure. Administration of the GABA receptor agonist, muscimol, into the lateral and third ventricles had no effect alone on pressure and HR prevented the cardiovascular effects of bicuculline, while the centrally active antihypertensive agent, clonidine, had no effect on bicuculline-induced increases in HR and pressure. The overall findings suggest that a tonically active GABAergic system exists in the region of the forebrain and exerts inhibitory control over sympathetic activity influencing arterial pressure and HR. 13 references. (Author abstract modified)

001613 Wilson, Charles J.; Fenster, Gary A.; Young, Stephen J.; Groves, Philip M. Dept. of Psychology, University of Colorado, Campus Box 345, Boulder, CO 80309 **Haloperidol-induced alteration of post-firing inhibition in dopaminergic neurons of rat substantia nigra.** *Brain Research*. 179(1):165-170, 1979.

Haloperidol (0.025mg/kg i.v.) increased the mean firing rate of 19 of 22 dopaminergic neurons recorded from the substantia nigra of immobilized male Sprague-Dawley rats. In many cases, a second injection produced a further increase in firing rate, but cumulative doses in an excess of 0.05mg/kg produced no further increase in rate. For all dopaminergic neurons tested, comparison of predrug and postdrug autocorrelation histograms revealed an apparent decrease in the strength or duration of post-firing inhibition. 16 references.

001614 Wood, J. D.; Tsui, D.; Phillis, J. W. Dept. of Biochemistry, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N 0W0 **Structure-activity studies on the inhibition of gamma-aminobutyric acid uptake in brain slices by compounds related to nipecotic acid.** *Canadian Journal of Physiology and Pharmacology*. 57(6):581-585, 1979.

Various N-methyl derivatives of nipecotic acid and related compounds were tested as inhibitors of gamma-aminobutyric acid (GABA) uptake into mini slices of whole mouse brain. N-Methylnipecotic acid, N,N-dimethylnipecotic acid, N-methylguvacine, and N-methylnicotinic acid were effective inhibitors. None of them, however, were as potent as nipecotic acid itself. All the effective inhibitors, including nipecotic acid, also inhibited the uptake of L-proline, but to a lesser extent. Four of the test compounds produced a depressant action on rat cerebral cortical neurons, but even N-methylisoguvacine, the most potent in this respect, was considerably less active than GABA. It is concluded that methylation of the N-atom of nipecotic acid and its derivatives was unlikely to lead to the development of agents with greater experimental or therapeutic potential than that of nipecotic acid itself, if the action of the agent was dependent on its effects on GABA uptake. 17 references. (Author abstract modified)

001615 Wood, Jeanette M.; Laverty, Richard. Dept. of Pharmacology, University of Otago Medical School, Dunedin, New Zealand **Effect of depletion of brain catecholamines on ethanol**

tolerance and dependence. *European Journal of Pharmacology*. 58(3):285-293, 1979.

Intraventricular 6-hydroxydopamine (6-OHDA) was used to deplete brain catecholamines in male Wistar rats subsequently fed a liquid diet containing ethanol. When ethanol was withdrawn, the withdrawal reactions were significantly more severe in the catecholamine depleted animals than in controls. Sleeping times after a standard dose of ethanol or pentobarbitone were significantly reduced in the 6-OHDA treated animals. The effects on sleeping time and withdrawal severity were not seen in animals specifically depleted of dopamine. Tolerance to the effects of prolonged ethanol administration was similar in 6-OHDA treated and control rats. Results suggest that the withdrawal and sleeping time responses in 6-OHDA treated rats were due to a nonspecific increase in CNS excitability resulting from depletion of noradrenaline. Central catecholamines apparently do not play a direct role in the development of ethanol tolerance and physical dependence. 33 references. (Author abstract modified)

001616 Wouters, W.; van den Bercken, J. Institute of Veterinary Pharmacology and Toxicology, University of Utrecht, Biltstraat 172, 3572 BP Utrecht, The Netherlands **Effects of met-enkephalin on slow synaptic inhibition in frog sympathetic ganglion.** *Neuropharmacology*. 19(3):237-243, 1980.

The influence of met-enkephalin on slow inhibitory postsynaptic potentials (IPSP) in the frog sympathetic ganglion was studied using a sucrose gap technique. A 1mcM dose caused a hyperpolarization of the ganglionic neurons, and the drug also depressed the amplitude of the slow IPSP by 40%. Both effects were completely antagonized by 1mcM naloxone. D-ala-met-enkephalinamide and morphine also produced a hyperpolarization together with a depression of the slow IPSP. The sensitivity of the ganglion to exogenous dopamine, the putative transmitter for the slow IPSP, was only slightly suppressed by met-enkephalin. It is concluded that slow IPSP depression by met-enkephalin is presynaptic in origin and may result from a decrease in the amount of transmitter released from the nerve terminals. The possibility that reduced transmitter release is caused by a hyperpolarization of the nerve terminals is also discussed. 37 references. (Author abstract modified)

001617 Wuster, Michael; Schulz, Rudiger; Herz, Albert. Dept. of Neuropharmacology, Max-Planck-Institut für Psychiatrie, Kraepelinstrasse 2, D-8000, Munich 40, Germany **Inquiry into endorphinergic feedback mechanisms during the development of opiate tolerance/dependence.** *Brain Research*. 189(2):403-411, 1980.

Endorphinergic feedback mechanisms during the development of opiate tolerance/dependence were investigated. Met-enkephalin and beta-endorphin levels were determined in the pituitary and brain of rats after treatment for several weeks with either agonists of high receptor affinity, such as levorphanol and etorphine, or with the narcotic antagonist naloxone. Long-term activation of opiate receptors failed to change the endorphin levels in restricted areas of brain and pituitary, although a high degree of tolerance/dependence was apparent in those animals. Chronic blockade of opiate receptors by naloxone fails to affect endorphin levels in the pituitary, but selectively increases met-enkephalin levels in the striatum. These results do not support the notion of negative feedback mechanisms to regulate endorphinergic functions during the development of opiate tolerance/dependence. 27 references. (Author abstract modified)

001618 Yim, Chi Yiu; Mogenson, Gordon J. Mogenson: Dept. of Physiology, Health Sciences Center, University of Western Ontario, London, Ontario, Canada N6A 5C1

Electrophysiological studies of neurons in the ventral tegmental area of Tsai. Brain Research. 181(2):301-313, 1980.

Extracellular recordings were obtained from single neurons in the ventral tegmental area (TA) of male Wistar rats anesthetized with urethane. The area contained two groups of neurons with distinctly different spike durations, firing rates, and firing patterns. One group had properties similar to those of nigral dopaminergic neurons (slow random firing rates, unusually long spike durations, and slow conduction velocities) and were believed to be A10 dopaminergic neurons. The other group had faster, rhythmical firing rates, short spike durations, and faster conduction velocities, indicating they were nondopaminergic. Units from both groups were antidromically activated by electrical stimulation of the nucleus accumbens, suggesting the nucleus accumbens receives dual projections of dopaminergic and nondopaminergic fibers from the VTA. The discharge rate of 141 of 142 neurons tested in the VTA was reduced by GABA, and this inhibition was blocked by picrotoxin. Picrotoxin alone activated 47.7% of the units tested. Results provide evidence of a GABA input to dopaminergic and nondopaminergic neurons projecting to the limbic forebrain structures. 32 references. (Author abstract modified)

001619 Yonhara, Norifumi; Matsuda, Tomohiro; Saito, Kihachi; Ishida, Hajime; Yoshida, Hiroshi. Dept. of Pharmacology 1, Osaka University School of Medicine, Nakanoshima 4-3-57, Kitaku, Osaka 530, Japan **Effect of cyclic nucleotide derivatives on the release of ACh from cortical slices of the rat brain.** Brain Research. 182(1):137-144, 1980.

Atropine (5nM to 5mM) produced a dose dependent enhancement of acetylcholine (ACh) release from male Sprague-Dawley rat brain cortical slices exposed to high potassium (K). Hexamethonium and D-tubocurarine had no effect on ACh release. The enhanced release induced by atropine was partially antagonized by oxotremorine (50 to 500 mM) or dibutyl cyclic GMP or 8-bromo-cyclic GMP (1 mM), but not by tetrodotoxin (200 nM) or dibutyl cyclic AMP (1 mM). The effects of oxotremorine and cyclic GMP derivatives were not due to diminished ACh synthesis, since these compounds did not influence the reduction of tissue ACh resulting from treatment with K and atropine. Results suggest that cyclic GMP may mediate the regulation of ACh release by presynaptic muscarinic receptors. 27 references. (Author abstract modified)

001620 Yoshida, Kazuhide; Kato, Yuzuru; Imura, Hiroo. Second Dept. of Internal Medicine, Faculty of Medicine, Kyoto University, Kyoto, Japan **Nicotine-induced release of noradrenaline from hypothalamic synaptosomes.** Brain Research. 182(2):361-368, 1980.

The release of tritiated noradrenaline (3H-NA) from male Wistar rat hypothalamic synaptosomes was increased by nicotine, carbamylcholine chloride, reserpine, or tyramine hydrochloride. Arecoline, atropine sulfate, and mecamlamine hydrochloride had no significant effect. Mecamlamine hydrochloride completely inhibited the nicotine or carbamylcholine-induced release of 3H-NA, but had no effect on reserpine or tyramine-induced release. Depolarization induced by high potassium concentration resulted in significantly enhanced release of 3H-NA. 16 references. (Author abstract modified)

001621 Young, W. Scott, III; Kuhar, Michael J. Kuhar. Dept. of Pharmacology, Johns Hopkins University School of Medicine, 725 North Wolfe St., Baltimore, MD 21205 **Noradrenergic alpha1 and alpha2 receptors: autoradiographic visualization.** European Journal of Pharmacology. 59(3/4):317-319, 1979.

Light microscopic autoradiographic methods were used to localize alpha-1 and alpha-2 receptors in intact tissue sections of

rat brain. Both types of receptors were widely distributed in brain. High densities of alpha-2 receptors (identified by p-aminoclonidine binding) were found in parts of the limbic system, arcuate nucleus, locus coeruleus, nucleus tractus solitarius, and lamina II of the spinal cord. High densities of alpha-1 receptors (identified by WB-4101 binding) were found in parts of the olfactory bulb and in the dentate gyrus of the hippocampus. 5 references.

001622 Yousufi, M. Ayub Khan; Thomas, John W.; Tallman, John F. Section on Biochemistry and Pharmacology, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Solubilization of benzodiazepine binding site from rat cortex.** Life Sciences. 25(5):463-470, 1979.

The high affinity binding site for (3H)diazepam has been solubilized from rat brain using .5% Lubrol-PX. Using a polyethylene glycol (PEG) gamma globulin assay, it has been possible to demonstrate solubilization of about 60% of the binding sites in a single step. The solubilized binding site possesses a KD of 11 nM for (3H)diazepam compared to approximately 4 nM for the membrane bound form, and binding is to a single class of sites. The order of potency of benzodiazepines is identical for the solubilized receptor and the membrane form. Binding of (3H)diazepam is temperature dependent and higher at 4 degrees than 37 degrees centigrade. Both urea and guanidine-HCL were capable of totally inhibiting binding, and this inhibition was partly reversible; neither sulfhydryl groups nor carbohydrate moieties seem to be important for binding. Gamma Aminobutyric acid which enhanced (3H)diazepam binding to membrane fractions was without effect on the solubilized binding site. 15 references. (Author abstract)

001623 Yutrzenska, G. J.; Davis, J. S.; Parmar, S. S. Parmar. Department of Physiology, University of North Dakota School of Medicine, Grand Forks, ND 58202 **Catecholamine mediation of the anticonvulsant activity of flurazepam.** Research Communications in Psychology, Psychiatry and Behavior. 5(1):2-12, 1980.

The role of central nervous system catecholamines as mediators of the anticonvulsant activity of flurazepam was investigated. Flurazepam, in doses of 1mg/kg and 2mg/kg, provided protection against pentylenetetrazol-induced seizures in male albino, CF1 mice. Pretreatment of the mice with either reserpine, alpha-methyl-p-tyrosine, L-dopa, phenoxybenzamine, or propranolol prior to administration of flurazepam provided a potentiation of the observed anticonvulsant activity of flurazepam. On the other hand, pretreatment with disulfiram produced essentially no change in the anticonvulsant activity of flurazepam. These observations provide evidence for a possible role of catecholaminergic pathways in the anticonvulsant activity of flurazepam. 28 references. (Author abstract)

001624 Zahniser, Nancy R.; Minneman, Kenneth P.; Molinoff, Perry B. University of Colorado Health Sciences Center, Dept. of Pharmacology, 4200 East Ninth Avenue, Denver, CO 80262 **Persistence of beta-adrenergic receptors in rat striatum following kainic acid administration.** Brain Research. 178(2-3):589-595, 1979.

The number and properties of beta-adrenergic receptors and their subtypes were determined following intrastriatal injection of kainic acid (KA) in male Sprague-Dawley rats. Results showed that striatal beta-adrenergic receptors persist even when neurons originating within the striatum are destroyed; the density of beta1-adrenergic and beta2-adrenergic receptors was not altered by KA administration. Results are consistent with a non-neuronal localization of striatal beta-adrenergic receptors, possibly on blood vessels or glial cells. 31 references.

001625 Zand, Robert; Izquierdo, Ivan. Dept. of Biological Chemistry, University of Michigan, Ann Arbor, MI 48109 **Anticonvulsant activity of cyclopentano amino acids**. *Neurochemical Research*. 5(1):1-7, 1980.

The hypothesis that certain amino acid analogues possessing a five membered ring structure or amino acid analogues that can be viewed as fragments derived from such a ring would have anticonvulsant activity was tested. The compounds 1-amino-cyclopentane carboxylic acid, 1-amino-3-methylcyclopentane carboxylic acid, 3-aminotetrahydrothiophene carboxylic acid, and alpha-aminoisobutyric acid were found to protect rats against seizures in the maximal electroshock test but offered no protection against metrazol (pentylenetetrazol) induced seizures in mice. The structural feature of this class of anticonvulsants that allows for hydrophobic interactions at the receptor site is considered to be a major physical factor necessary in promoting the activity of this class of anticonvulsants. 23 references. (Author abstract modified)

001626 Zatz, Martin. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Pharmacology of the rat pineal gland**. (Unpublished paper). Bethesda, MD, NIMH, 1979. 33 p.

Some of the effects of drugs on pineal metabolism, with particular emphasis on the pineal metabolism of the rat, are described. Areas covered include: sympathomimetics and related agents, inhibitors of protein or ribonucleic acid (RNA) synthesis, cations, and psychoactive drugs. Also discussed are agents which affect presynaptic functions, mimic the effects of light, change cyclic guanylic acid (GMP) levels, or change phospholipid metabolism. 94 references.

001627 Zatz, Martin. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Resetting the biological clock with light and drugs**. (Unpublished paper). Bethesda, MD, NIMH, 1980. 1 p.

The two effects of light on the rat pineal gland are discussed: 1) an acute, suppressive effect; and 2) a phase shifting or entraining effect. The acute effect can be seen in less than one cycle and can be mimicked by a number of peripherally and centrally active drugs. An example of a drug which mimics the acute effect of light on the pineal without acting on the circadian oscillator is propranolol. In contrast, the phase shifting effect of light requires observations over a number of cycles and, as a change in temporal pattern, necessarily reflects a change in the driving oscillator. An important property of the circadian oscillator is that its response to light is itself phase dependent. Pulses of light can cause phase delays, phase advances, or can have no effect, depending on when they are applied in the free running rhythm. These phase shifting effects of light provide a paradigm for drug action on the circadian pacemaker. Acutely administered drugs which cause phase shifts in free running rhythms must be affecting the circadian oscillators. An example of such a drug is carbachol. Depending on the phase at which the drug is given, carbachol caused phase delays or phase advances in the free running rhythms. These data raise the possibility of a role for acetylcholine in the effect of light on the mammalian circadian pacemaker. (Author abstract modified)

001628 Zetler, Gerhard. Institut für Pharmakologie der Medizinischen Hochschule Lubeck, Ratzeburger Allee 160, D-2400 Lubeck, Germany **Antagonism of cholecystokinin-like peptides by opioid peptides, morphine or tetrodotoxin**. *European Journal of Pharmacology*. 60(1):67-77, 1979.

Morphine, beta-endorphin, met-enkephalin, and leu-enkephalin antagonized the action of cholecystokinin octapeptide (CCK-8), caerulein, and pentagastrin in guinea-pig ileum in a manner suggesting physiological competitive antagonism. Angiotensin was much less sensitive than the acidic peptides to the actions of

opioids. Naloxone did not modify the response to CCK-8 and caerulein, but completely abolished the antagonistic influence of the opioids. It is suggested that opioid and CCK-like peptides in gut and brain interact in the regulation of intestinal motility and satiety. 54 references. (Author abstract modified)

001629 Zieher, Luis Maria; Jaim-Etcheverry, Guillermo. Jaim-Etcheverry: Catedra de Farmacologia, Facultad de Medicina, Paraguay 2155, 1121 Buenos Aires, Argentina **6-Hydroxydopamine during development: relation between opposite regional changes in brain noradrenaline**. *European Journal of Pharmacology*. 58(3):217-223, 1979.

The contribution of forebrain denervation to the elevation of noradrenaline (NA) in the brainstem and cerebellum of Wistar rats treated with 6-hydroxydopamine (6-OHDA) at birth was examined. Intraventricular administration of 12.5 to 50mcg 6-OHDA produced a long-lasting elevation of NA in brainstem and cerebellum and a reduction of NA in cortex and spinal cord. However, a 75mcg dose of 6-OHDA reduced cortical and spinal NA without increasing NA in the brainstem and cerebellum. Systemic injection of 6-hydroxydopa at 3 days of age increased brainstem NA to a comparable extent in rats treated with 75mcg 6-OHDA at birth and in control rats. Results suggest that forebrain denervation is not the sole stimulus responsible for triggering processes leading to the increase of NA in the brainstem. 20 references. (Author abstract modified)

001630 Zis, Athanasios P.; Marangos, Paul J.; Parma, Alexandra M.; McGeer, Edith G. Clinical Studies Unit, University Hospital APH 6, Dept. of Psychiatry, 1405 East Ann Street, Ann Arbor, MI 48109 **Changes in striatal neuron-specific enolase (NSE) and non-neuronal enolase (NNE) following kainic acid administration**. *Brain Research*. 183(2):486-489, 1980.

The effects of kainic acid (KA) injections on striatal neuron specific enolase (NSE) and nonneuronal enolase (NNE) were investigated. Groups of male albino rats were injected stereotactically with 5nM of KA into the left corpus striatum and sacrificed 24 and 72 hours, and 8 and 9 days posttreatment. KA injection decreased NSE significantly more than NNE. Results are consistent with both the presumed selectivity of KA lesions as well as the time course of its effects. It is noted that the possibility that some glial damage, undetected by crude morphological means, does actually precede gliosis, cannot be excluded. This hypothesis would explain the decrease in NNE. Alternatively, the small yet significant decrease in NNE may, like the decrease in NSE, also be the result of neuronal rather than glial damage. 11 references.

04 MECHANISM OF ACTION: BEHAVIORAL

001631 Abel, E. L.; Day, N.; Dintcheff, B. A.; Ernst, C. A. S. Research Institute on Alcoholism, Buffalo, NY 14203 **Inhibition of postnatal maternal performance in rats treated with marijuana extract during pregnancy**. *Bulletin of the Psychonomic Society*. 14(5):353-354, 1979.

Whether treatment of adult rats with marijuana during pregnancy would affect postnatal development of nondrug exposed neonates assigned to them was examined. Ss were 68 primiparous Long-Evans rats treated either with a crude marijuana extract or olive oil, or left untreated. Results show that neonatal rats raised by dams treated with marijuana extract during pregnancy gained less weight and reared significantly less in an open-field than neonates raised by nondrug treated dams. 4 references. (Author abstract modified)

001632 Akins, Faren R.; Gouvier, William Drew; Lyons, Joseph E. Gouvier: Dept. of Psychology, Memphis State University, Memphis, TN 38152 **Stimulus control along a drug-dose**

dimension. *Bulletin of the Psychonomic Society.* 15(1):33-34, 1980.

Stimulus control along a drug dose dimension was examined. Pigeons were trained to discriminate between two dosage levels of phenobarbital, each associated with a different density of reinforcement. Postdiscrimination generalization testing revealed stimulus control exerted along the drug dosage dimension. Two of four subjects produced gradients showing a peak shift. The results support the notion that drug produced interoceptive stimuli can acquire discriminative properties analogous to those observed using similar training with exteroceptive stimulus dimensions. 7 references. (Author abstract modified)

001633 Alexander, George J.; Chatterjee, Nithiananda. Neurotoxicology Research Unit, New York State Psychiatric Institute, New York, NY 10032 **Anticonvulsive activity of indenoimidazolidinones and related heterocyclic compounds in mice.** *Research Communications in Chemical Pathology and Pharmacology.* 27(1):45-56, 1980.

A series of substituted cyclic ureides and related compounds was synthesized by condensing ninhydrin with urea, thiourea, dimethylurea, or other aromatic or bifunctional agents. When tested against audiogenic or metrazol-induced seizures in male albino mice, four compounds decreased the incidence or severity of convulsive manifestations and protected against mortality. The effective compounds were not toxic at the dose used (150mg/kg) and produced few observable sedative effects. 8 references. (Author abstract modified)

001634 Amir, Shimon; Amit, Zalman. Dept. of Psychology, Concordia University, 1455 de Maisonneuve Blvd. W., Montreal, Quebec, Canada H3G 1M8 **Enhanced analgesic effects of stress following chronic administration of naltrexone in rats.** *European Journal of Pharmacology.* 59(1/2):137-140, 1979.

Chronic administration of the long acting opiate antagonist naltrexone potentiated the analgesic effects of foot shock stress in the hot plate test in male Wistar rats. No changes in pain responsiveness were noted in naltrexone treated rats that were not subjected to the foot shock treatment. Results suggest that chronic opiate receptor blockade may lead to the development of supersensitivity in endogenous opiate systems that mediate the analgesic effects of stress. 16 references. (Author abstract)

001635 Amir, Shimon; Blair, Richard; Amit, Zalman. Center for Research on Drug Dependence, Dept. of Psychology, 1455 de Maisonneuve Blvd. West Montreal, Quebec, H3G 1M8, Canada **Increased amphetamine potency following chronic naltrexone administration in rats.** *Life Sciences.* 25(16):1407-1412, 1979.

The amphetamine and apomorphine-induced stimulation of locomotor activity in male Wistar rats was potentiated by chronic pretreatment with naltrexone, a long-acting opiate antagonist. Chronic naltrexone treatment also resulted in increased locomotor activity in saline injected rats. Results suggest that chronic opiate receptor blockade may lead to the development of supersensitivity in dopamine systems that mediate motor control and that endogenous opioids modulate the functions of these systems. 46 references. (Author abstract modified)

001636 Anisman, Hymie; Suissa, Albert; Sklar, Lawrence S. Dept. of Psychology, Carleton University, Ottawa, Ontario K1S 5B6, Canada **Escape deficits induced by uncontrollable stress: antagonism by dopamine and norepinephrine agonists.** *Behavioral and Neural Biology.* 28(1):34-47, 1980.

Exposure to inescapable shock was found to retard escape performance of mice tested 24 hours later in a modified shuttle task. In accordance with the view that depletion of norepinephrine

and dopamine contribute to this effect, the dopamine receptor agonist, apomorphine, and the norepinephrine receptor agonist, clonidine, antagonized the performance disruption. This was the case regardless of whether the drugs were administered prior to inescapable shock or prior to test. These drug effects could neither be attributed to state dependent effects nor to residual drug action. The data support the contention that the disruption of escape behavior after inescapable shock is due to deficits of response maintenance mediated by dopamine and norepinephrine depletion, rather than to learned helplessness. 24 references. (Author abstract)

001637 Antelman, Seymour M.; Eichler, Alan J.; Black, Cynthia A.; Kocan, Donna. University of Pittsburgh School of Medicine, Pittsburgh, PA **Interchangeability of stress and amphetamine in sensitization.** *Science.* 207(4428):329-331, 1980.

The hypothesis that presentation of a stressor, mild tail pressure (TP), can sensitize an animal to the later effects of amphetamine and vice versa was tested. Male Sprague-Dawley rats were subjected to a program of TP trials. After the completion of the TP regimen, the animals were injected with a d-amphetamine sulfate. The results support the hypothesis and suggest that amphetamine and at least some stressors may be interchangeable in their ability to induce sensitization. It is suggested that the data raise the possibility that stress might be a common variable contributing to both amphetamine psychosis and some forms of schizophrenia. 16 references. (Author abstract modified)

001638 Atterwill, C. K.; Green, A. R. MRC Unit and University Dept. of Clinical Pharmacology, Radcliffe Infirmary, Woodstock Road, Oxford, England **Responses of developing rats to L-tryptophan plus an MAOI - I. Monitoring changes in behaviour, brain 5-HT and tryptophan.** *Neuropharmacology.* 19(4):325-335, 1980.

The behavioral responses of developing (21-day-old) and adult (40 to 50-day-old) rats to tranlycypromine (an MAOI) plus L-tryptophan (L-TP) were monitored. The concomitant changes in whole brain 5-HT levels and tryptophan concentration were also measured. Following tranlycypromine (TCP), L-TP administration produced a characteristic hyperactivity syndrome in both groups. Differences in brain 5-HT and tryptophan accumulation between adults and pups were noted following L-TP injection. The 21-day-old rat brain tryptophan accumulation was greater than that of adult brain at all doses of L-TP, the difference becoming greater as the L-TP dose was increased. In contrast, 21-day-old brain 5-HT accumulation plateaued at a lower dose of L-TP and a lower total brain tryptophan concentration than the adult brain, whose accumulation continued to increase up to doses of 11mcg/kg, as previously observed. No difference in sensitivity postsynaptic to the 5-HT neurons was found between adult and immature rats using the putative 5-HT receptor agonists 5-methoxy-N,N-dimethyltryptamine (5-MeODMT) or quipazine. Prevention of the peripheral decarboxylation of L-TP to tryptamine using benserazide drastically reduced the activity of 21-day-old rats to TCP plus L-TP administration. Whether the predominant participation of tryptamine in the immature rat behavioral responses to L-TP administration can explain the increasing activity without an increase in brain 5-HT accumulation, or whether some other factor can explain this discrepancy remains to be determined. 38 references. (Author abstract)

001639 Atterwill, C. K.; Green, A. R. MRC Unit and University Dept. of Clinical Pharmacology, Radcliffe Infirmary, Woodstock Road, Oxford, England **Responses of developing rats to L-tryptophan plus an MAOI - II. Effects of repeated electroconvulsive shock.** *Neuropharmacology.* 19(4):337-341, 1980.

The effects of administration of repeated electroconvulsive shock (ECS) to developing rats from days 10 to 20 on behavioral responses to tranlycypromine (TCP) plus L-tryptophan (L-TP) injection on day 21 were investigated. In addition to a 14% increase in behavioral response to TCP plus L-TP, there was also an increase in the total number of recorded movements on the Animex activity meters in the ECS pretreated group (30%) over controls but this failed to reach statistical significance. Further, responses to the agonist 5-methoxy-N,N-dimethyl-tryptamine (5-MeODMT) were also significantly enhanced (67%). This suggests that a fully developed CNS is not necessary for the induction of these behavioral changes in the rat brain 5-HT system. There were essentially no differences between control and electroshocked groups in 5-HT synthesis rate (measured by accumulation of 5-HT following an MAOI), tryptophan concentration, or 5-HIAA concentration. The chronic ECS treatment also resulted in a decreased rate of growth of the immature rats. 19 references. (Author abstract modified)

001640 Aulakh, C. S.; Bhattacharyya, A. K.; Hossain, M. A.; Pradhan, S. N. Dept. of Pharmacology, College of Medicine, Howard University, Washington, DC **Behavioral and neurochemical effects of repeated administration of delta9-tetrahydrocannabinol in rats.** *Neuropharmacology*. 19(1):97-102, 1980.

The effects of repeated administration of delta9-tetrahydrocannabinol (THC, 10mg/kg i.p., twice daily at 8 hour intervals) on spontaneous motor activity (SMA) and neurotransmitter levels in various brain regions were determined in male Wistar rats. In the first hour after the first dose of THC, decreases were seen in SMA, in dopamine levels in the diencephalon/midbrain (DM) and caudate nucleus, and in norepinephrine levels in the DM and pons-medulla (PM); 5-hydroxytryptamine levels in the DM and PM were increased. These behavioral and neurochemical changes were enhanced by daily injections of THC up to day 5 and then gradually returned to normal. Behavioral changes observed during the second hour after THC injection could also be correlated with regional alterations in neurotransmitter levels. 33 references. (Author abstract modified)

001641 Babbini, M.; Gaiardi, M.; Bartoletti, M. Institute of Pharmacology, University of Bologna, I-40126 Bologna, Italy **Stimulus-response relationships in a quickly learned escape from shock: effects of morphine.** *Pharmacology Biochemistry and Behavior*. 11(2):155-158, 1979.

The relationship between stimulus (shock) intensity and analgesic effectiveness of morphine was investigated in rats by means of an operant technique. Under control conditions, a good linear relationship between the log of stimulus intensity and the log of speed to press the lever was found. Morphine showed inhibitory effects upon this escape behavior, which were greater at any given dose with greater intensity of the shock. These effects were dose related: the slopes of the shock response lines decreased with increasing dose. Data do not appear to be a consequence of a general depressant effect of the drug on behavior, and are in line with several experimental observations showing that in animals, as well as humans, the magnitude of the analgesic effect of morphine tends to increase as pain severity increases. 19 references. (Author abstract modified)

001642 Baettig, Karl; Martin, James R.; Classen, Werner. Institut für Verhaltenswissenschaft, ETH-Zürich, Turnerstrasse 1, CH-8092 Zurich, Switzerland **Nicotine and amphetamine: differential tolerance and no cross-tolerance for ingestive effects.** *Pharmacology Biochemistry and Behavior*. 12(1):107-111, 1980.

The effects of semichronic nicotine administration on body weight and ingestive behavior were compared with those of amphetamine, and cross-tolerance for the two drugs was evaluated. Rats chronically treated twice daily with nicotine or d,l-amphetamine exhibited different patterns of anorexia, hypodipsia, and body weight loss. Amphetamine treated rats developed tolerance to these ingestive effects and to weight loss, whereas nicotine injected rats did not. There was little, if any, evidence for cross-tolerance when the drugs were switched between the two groups. These results indicate that different mechanisms underlie the ingestive effects of nicotine and amphetamine. 48 references. (Author abstract modified)

001643 Baltzer, V.; Huber, H.; Weiskrantz, L. Research Department, Pharmaceuticals Division, CIBA-GEIGY, Ltd., Basel, Switzerland **Effects of various drugs on behavioral contrast using a double-crossover procedure.** *Behavioral and Neural Biology*. 27(3):330-341, 1979.

A behavioral contrast method that yields reliable and durable effects in both the positive and negative directions in the same animals was used to test the effects of sodium amylbarbitone, maprotiline, chlordiazepoxide, pargyline, diazepam, imipramine, chlorpromazine, and D-amphetamine. A new graphical method is described that allows presentation of all the relevant within day and between day data in a single display, as well as detection of changes in size of positive and negative contrast. The two minor tranquilizers, chlordiazepoxide and diazepam, as well as amylbarbitone, produced significant reductions in positive and negative contrast with the negative ones being more conspicuous. The results suggest that the minor tranquilizers, including amylbarbitone may be more adequately described as having an emotional flattening effect, rather than a restricted anti-anxiety or anti-frustration action. 10 references. (Author abstract modified)

001644 Barragan, L. A.; Delhaye-Bouchaud, N. Delhaye-Bouchaud: Lab. de Neurophysiologie ontogenetique, Universite P. et M. Curie, 4, place Jussieu, F-75230 Paris Cedex 05, France **Harmaline-induced activation of the olivo-cerebellar system in young rabbits: further evidence for a transient multi-innervation of Purkinje cells by climbing fibres.** *Neuropharmacology*. 19(3):305-310, 1980.

Ontogenetic evolution of behavioral and electrophysiological responses to harmaline was studied in the maturing rabbit. Harmaline-induced tremor could not be elicited before the second postnatal week, but as soon as it appeared, no significant difference was seen in its intensity compared with the adult animal. Electrophysiological studies of cerebellar Purkinje cell activity revealed a similar age dependence since no rhythmic firing of climbing fiber responses was found before the eighth postnatal day. In addition, harmaline activation revealed a transient multiple innervation of Purkinje cells by climbing fibers. It is suggested that the presence of serotonergic fibers is critical for the effects of harmaline to develop. 34 references. (Author abstract modified)

001645 Barry, H., III; Krimmer, E. C. Dept. of Pharmacology, University of Pittsburgh School of Pharmacy, Pittsburgh, PA 15261 **Differential stimulus attributes of chlordiazepoxide and pentobarbital.** *Neuropharmacology*. 18(12):991-998, 1979.

The discriminative stimulus properties of tranquilizers and sedatives are compared, based on data obtained with chlordiazepoxide (CDP) and pentobarbital (PENT) as prototype drugs. Studies of discriminative stimulus properties of drugs are more sensitive to the effects of therapeutic doses than most animal behavior models. In drug discrimination studies, rats trained to discriminate CDP or PENT from saline subsequently choose the

drug rather than nondrug condition when tested with the alternate drug. Rats are also able to discriminate the effects of CDP from those of PENT in this procedure. Dose/response studies suggest that the disinhibitory or behaviorally stimulant effects of CDP are primarily due to emotional relaxation, while those of PENT are due to impaired motor control. Both drugs appear to be more similar to each other than to ethyl alcohol. In rats trained to discriminate CDP from PENT, the alcohol cue was more similar to CDP during restricted movement but more similar to PENT during vigorous movement. 34 references. (Author abstract modified)

001646 Bartus, Raymond T. Medical Research Division, American Cyanamid Company, Pearl River, NY 48106 **Physostigmine and recent memory: effects in young and aged nonhuman primates.** *Science*. 206(4422):1087-1089, 1979.

The effect of physostigmine on recent memory was evaluated in four young (5 to 7 years old) and eight aged (over 18 years old) rhesus monkeys. All aged monkeys had previously shown impaired memory. The performance of young monkeys treated with physostigmine was similar to that reported in young humans: no effects at low doses, some improvement at a restricted dose range, and deficits at the highest dose. Although the aged monkeys also improved at the same general doses, their overall response as a group was much more variable. Performance of some aged monkeys was impaired by low doses that did not effect young monkeys. Continued improvement was observed in some aged monkeys at the highest dose, which typically impaired young monkeys. These variable effects across age suggest that physostigmine can not reliably be used to treat geriatric cognition. Results suggest that appropriated manipulation of the cholinergic system may eventually be developed to alleviate some of the cognitive impairment suffered by the aged. 15 references. (Author abstract)

001647 Bartus, Raymond T. CNS Biology, American Cyanamid Company, Medical Research Division, Lederle Laboratories, Pearl River, NY 10965 **Four stimulants of the central nervous system: effects on short-term memory in young versus aged monkeys.** *Journal of the American Geriatrics Society*. 27(7):289-297, 1979.

Aged Rhesus monkeys and young control monkeys were tested in a delayed response procedure to assess the effects of CNS stimulants on short-term memory (STM). Four different doses of each of four CNS stimulants (methylphenidate, magnesium pemoline, a pentylenetetrazole/niacin mixture, and caffeine) were given to each monkey counterbalanced for possible order effects. Methylphenidate and caffeine impaired the performance of both age groups in this nonhuman primate cognitive task, even at relatively low dose levels. Magnesium pemoline produced fewer adverse effects and some evidence of improving STM in the aged monkeys, although not within the levels of statistical significance. The pentylenetetrazole/niacin mixture produced a three way interaction involving age, dose, and retention interval. This reflected the fact that statistically significant aged related deficits did occur in the STM dependent retention interval as the dose varied. The data demonstrate that, of these four CNS stimulants, none readily improves (and often may impair) performance of tasks requiring STM. Therefore, the results of this study offer little support for the hypothesis that general CNS stimulation may constitute significant therapy for cognitive impairments associated with advanced age. 30 references. (Author abstract modified)

001648 Batty, Jennifer; Meyerson, Bengt J. Dept. of Medical Pharmacology, University of Uppsala, Uppsala, Sweden **The effects of p-chlorophenylalanine, fenfluramine and alpha-methyltyrosine on marking responses in the male Mongolian gerbil (Mer-**

iones unguiculatus). *Pharmacology Biochemistry and Behavior*. 12(2):181-184, 1980.

Marking behavior was maintained by testosterone propionate (TP) treatment in castrated Mongolian gerbils. Responses were enhanced by p-Chlorophenylalanine (PCPA) and inhibited by alpha-methyltyrosine (AlphaMT). No effect was seen by PCPA in subjects not treated with TP. Fenfluramine inhibited the response in intact gerbils. The data suggest that serotonergic inhibitory mechanisms exist which are impaired in testosterone dependent marking behavior in the Mongolian gerbil. 15 references. (Author abstract)

001649 Beatty, William W.; Shavalia, David A. Dept. of Psychology, North Dakota State University, Fargo, ND 58105 **Spatial memory in rats: time course of working memory and effect of anesthetics.** *Behavioral and Neural Biology*. 28(4):454-462, 1980.

Working memory for spatial information was studied in an eight arm maze by imposing a delay of variable length between the animals' fourth and fifth choices. In all five rats tested memory was nearly perfect for delays of 60 sec to 4 hours. At longer delays memory declined systematically, although some evidence of memory persisted for 24 hours, the longest delay examined. Exposure to narcotizing doses of barbiturate anesthetics during the delay interval did not disrupt spatial memory. It is suggested that the long duration of nearly perfect memory in this situation should provide a useful procedure for assessing the effects of pharmacological and other reversible treatments on memory. 12 references. (Author abstract)

001650 Beleslin, D. B.; Samardzic, Ranka. Dept. of Pharmacology, Medical Faculty, Beograd 11000, P. O. Box 662, Yugoslavia **Effects of para-chlorophenylalanine and 5,6-dihydroxytryptamine on aggressive behaviour evoked by cholinomimetics and anticholinesterases injected into the cerebral ventricles of conscious cats.** *Neuropharmacology*. 18(3):251-257, 1979.

Intracerebroventricular injections of carbachol, muscarine, eserine, and neostigmine in conscious cats evoked emotional behavior, aggression, autonomic and motor phenomena, and clonic/tonic convulsions. In cats pretreated with 5,6-dihydroxytryptamine and parachlorophenylalanine, the affective type of aggressive behavior elicited by the cholinomimetics and anticholinesterases was modified; biting attack was prominent, and vocalization was depressed or absent. Hissing and snarling reappeared when 5-hydroxytryptophan was given to the cats treated with parachlorophenylalanine. Results suggest that an intact central serotonergic network is required for the expression of emotional behavioral phenomenon such as aggressive vocalization, but not for the performance of associated motor acts such as biting. 34 references. (Author abstract modified)

001651 Berntson, G. G.; Berson, B. S. Ohio State University, 1314 Kinnear Road, Columbus, OH 43121 **Antinociceptive effects of intraventricular of systemic administration of vasopressin in the rat.** *Life Sciences*. 26(6):455-459, 1980.

The effects of intraventricular administration of lysine-vasopressin on pain sensitivity in the rat were determined in the tail flick test. Vasopressin was found to induce potent and dose dependent antinociceptive actions, lasting up to 1 hour. An additional experiment demonstrated that analgesia induced by vasopressin was not blocked by naloxone, suggesting that this analgesia is independent of opiate receptor systems. Vasopressin was also found to be equally effective in elevating tail flick latency after systemic administration. It is suggested that vasopressin systems have a possible role in the regulation of pain sensitivity. 15 references. (Author abstract)

001652 Best, Michael R.; Domjan, Michael. Department of Psychology, Southern Methodist University, Dallas, TX 75275 **Characteristics of the lithium-mediated proximal US-preexposure effect in flavor-aversion conditioning.** *Animal Learning & Behavior*. 7(4):433-440, 1979.

The disruption of taste aversion learning in rats by exposure to the unconditioned stimulus (US), lithium, shortly before the conditioning trial was explored. Experiment 1 showed that the time course of the interference with conditioning is directly related to the preexposure drug dose. Experiment 2 demonstrated that the interference effect is evident even if the test for aversion learning is conducted following a drug injection, thereby minimizing stimulus generalization decrement for the preexposed subjects. Finally, Experiment 3 showed that disruption of the contingent relationship between tastes and drug effects is probably not responsible for the proximal US preexposure phenomenon because the interference with conditioning occurs regardless of whether or not the preexposure drug treatment is paired with a novel flavor. These findings, together with previous research, demonstrate the remarkably robust character of the proximal US preexposure phenomenon. 21 references. (Author abstract modified)

001653 Bhattacharyya, A. K.; Aulakh, C. S.; Pradhan, Sikta; Ghosh, P.; Pradhan, S. N. Dept. of Pharmacology, College of Medicine, Howard University, Washington, DC **Behavioral and neurochemical effects of delta-9-tetrahydrocannabinol in rats.** *Neuropharmacology*. 19(1):87-95, 1980.

The effects of delta-9-tetrahydrocannabinol (THC) on spontaneous motor activity (SMA), barbiturate sleeping time, rectal temperature, neurotransmitter levels, and self-stimulation (SS) were examined in male Wistar rats with electrodes implanted in the posterior hypothalamus or area ventralis tegmentum. A prolonged, generalized depression in SS responding in nonaroused rats was observed, accompanied by hypothermia and enhanced barbiturate sleeping times. However, a triphasic effect (depression/stimulation/depression) was seen for SS in aroused rats and for SMA. The effects of amphetamine and cocaine were antagonized during the initial depression, but were unaffected or potentiated during the subsequent stimulant phase. Neurochemical studies showed an initial decrease in dopamine (DA) in the caudate nucleus and diencephalon/midbrain (DM) and an increase of serotonin (5-HT) in DM and pons-medulla; this was followed by an increase in DA levels and a decrease in 5-HT levels, and finally a return to normal levels. 33 references. (Author abstract modified)

001654 Biagi, G. L.; Barbaro, A. M.; Guerra, M. C.; Babbini, M.; Gaiardi, M.; Bartoletti, M.; Borea, P. A. Istituto di Farmacologia, Università di Bologna, Bologna, Italy **Rm values and structure-activity relationship of benzodiazepines.** *Journal of Medicinal Chemistry*. 23(2):193-201, 1980.

Quantitative structure/activity relationships (QSAR) have been formulated for the activities of a series of benzodiazepines in rats. The lipophilic character of molecules was expressed by means of the chromatographic *Rm* values which were very well correlated with experimental or calculated log *P* values. The ideal lipophilic character for activity of benzodiazepines in the exploratory behavior test is not far from that of compounds acting in the CNS as unspecific depressant agents. Results of both the conflict and exploratory behavior studies might support the hypothesis of different sites of action for the anxiolytic and sedative effects of benzodiazepines. 34 references. (Author abstract)

001655 Blaustein, Jeffrey D.; Feder, Harvey H. Dept. of Zoology, Science Building II, Iowa State University, Ames, IA

50011 **Cytoplasmic progesterin receptors in female guinea pig brain and their relationship to refractoriness in expression of female sexual behavior.** *Brain Research*. 177(3):489-498, 1979.

Cytoplasmic progesterin receptors were assayed in the midbrain and hypothalamus/preoptic area/septum (HPS) of ovariectomized Hartley guinea-pigs given sequential treatment with estradiol benzoate (EB) and progesterone. When injected 40 hours after EB in a dose as low as 50mcg, progesterone caused a failure to display lordosis in response to a second progesterone injection 24 hours later, accompanied by a decrease in the concentration of cytoplasmic progesterin receptors in the HPS and midbrain. When given concurrently with 1.6mcg EB, a 500mcg dose of progesterone suppressed behavioral responsiveness to a second progesterone injection 40 hours later and decreased the concentration of available cytoplasmic progesterin receptors in HPS and midbrain; a low dose (100mcg) of progesterone had no effect. 38 references. (Author abstract modified)

001656 Boland, Frederick J.; Stern, Muriel H. Dept. of Psychology, Queen's University, Kingston, Ontario, Canada K7L 3N6 **Suppression by lithium of voluntary alcohol intake in the rat: mechanism of action.** *Pharmacology Biochemistry and Behavior*. 12(2):239-248, 1980.

Suppression by lithium of voluntary alcohol intake was studied using 70 Wistar rats showing either low preference for aversive alcohol solutions or a high preference induced by hypothalamus stimulation. A large lithium chloride injection suppressed alcohol intake only if alcohol was tasted. Pairing lithium contiguously with water or intubed alcohol failed to reduce subsequent alcohol intake despite the concurrent presence of high serum lithium levels. A series of seven lithium injections increased rather than decreased alcohol intake if lithium was allowed to accumulate in the blood and brain during alcohol exposure while the transitory sickness associated with each injection was prevented from association with the taste of alcohol. When sickness was allowed to occur during alcohol exposure a suppression of intake resulted after two injections. Contrary to current interpretations these results suggest that the suppression of voluntary alcohol intake by acute and chronic lithium administration is due to a learned taste aversion rather than to a pharmacological mechanism specific to alcohol. 53 references. (Author abstract)

001657 Borsini, F.; Bendotti, C.; Carli, M.; Poggesi, E.; Samanin, R. Istituto di Ricerche Farmacologiche Italy **The roles of brain noradrenaline and dopamine in the anorectic activity of diethylpropion in rats: a comparison with d-amphetamine.** *Research Communications in Chemical Pathology and Pharmacology*. 26(1):3-11, 1979.

The anorectic activity of diethylpropion and d-amphetamine was studied in female rats subjected to various treatments known to affect brain monoamines. The anorectic effects of both drugs were completely prevented by lesion of the ventral noradrenergic bundle, which selectively decreases brain noradrenaline, but were not significantly modified in rats treated with i.p. desipramine and intraventricular 6-hydroxydopamine to selectively deplete dopamine. Pretreatment with penfluridol significantly reduced the effect of d-amphetamine but not that of diethylpropion. Lesion of the nucleus medianus raphe, which destroys central serotonin neurons, or treatment with methergoline, a central serotonin antagonist, caused no changes in the effects of either compound. 28 references. (Author abstract modified)

001658 Bowman, Robert E.; Heironimus, Mark P.; Harlow, Harry F. University of Wisconsin, Psychology Primate Laboratory, Madison, WI 53706 **Pentylentetrazol: Posttraining injec-**

tion facilitates discrimination learning in rhesus monkeys. *Physiological Psychology*. 7(3):265-268, 1979.

The question whether learning enhancement by stimulant drug operates in the primate was studied. Rhesus monkeys given immediate posttraining injections of pentylenetetrazol (PTZ) exhibited improved acquisition of difficult discrimination learning problems but not of easy problems. Optimal facilitation occurred at a dosage of 10mg/kg. In two further experiments the interval between training and the injection of 10mg/kg of PTZ was varied and optimal facilitation occurred at the 1 minute interval. At the 30 minute interval, facilitation was absent and error rates were as high as the saline controls, but at the 60 minute interval a lower error rate was again seen. All findings were remarkably similar to those previously reported in mice, suggesting a common mechanism for the effect of PTZ on simple discrimination learning in both species. Through the use of the monkey, the potential enhancement of more complex learning by drugs is now accessible to investigation. 12 references. (Author abstract modified)

001659 Bowman, Robert E.; Heironimus, Mark P.; Fobes, Jim; Leary, Robert W.; Harlow, Harry F. Department of Psychology, Primate Laboratory, University of Wisconsin, Madison, WI 53706 **Facilitation of discrimination learning but not of learning set by post-training injections of pentylenetetrazol in rhesus monkeys.** *Behavioral and Neural Biology*. 28(1):89-98, 1980.

Three experiments on facilitation of learning by pentylenetetrazol (PTZ) were done with rhesus monkeys. The first of these replicated earlier findings of facilitation of single problem discrimination learning, this time using 15 rather than 2 minute training sessions before immediate injection of 10mg/kg of PTZ. Two subsequent experiments used 15 minute training sessions followed by PTZ injection in a learning set paradigm. Both the PTZ and the saline control groups acquired learning sets but the trends suggesting drug facilitation of this capacity were nonsignificant. It is suggested that a ceiling effect could have attenuated any facilitatory influences on between problem learning on this simple learning set. 10 reference. (Author abstract)

001660 Brady, Kathleen T.; Balster, Robert L.; Meltzer, Leonard T.; Schwartz, Dorie. Balster: Box 613, Medical College of Virginia, Richmond, VA 23298 **Comparison of phencyclidine and three analogues on fixed-interval performance in rhesus monkeys.** *Pharmacology Biochemistry and Behavior*. 12(1):67-71, 1980.

The effects of four arylcyclohexylamines on operant performance in rhesus monkeys were compared. Four rhesus monkeys were trained to lever-press on a multiple fixed-interval 5 minute/time out 1 minute schedule of food presentation during daily 1.5 hour sessions. Dose/response curves and median effective doses were determined for phencyclidine, N-ethyl-1-phenylcyclohexylamine, 1-(1-(2-thienyl) cyclohexyl) piperidine and ketamine. Ketamine was found to be approximately 1/10 as potent as the other drugs which were approximately equipotent. The drugs had qualitatively similar effects. High doses of all four drugs decreased overall response rates and the slopes of the dose/response curves were comparable. A dose related rate dependent effect was found for all four drugs. Onset and duration of the drug effects are described. 21 references. (Author abstract)

001661 Braff, David L.; Geyer, Mark A. Department of Psychiatry, School of Medicine, University of California, San Diego, M-003, La Jolla, CA 92139 **Acute and chronic LSD effects on rat startle: data supporting an LSD-rat model of schizophrenia.** (Unpublished paper). Research Report, NIMH Grant 1P50-MH-30914, 1979. 13 p.

The effects of acute and chronic LSD on measures of rat startle, a widely used behavioral measure of reactivity and habituation, were studied. Experiments were conducted to test the argument against the LSD animal model for human schizophrenia that while schizophrenia can be chronically debilitating, animal and human effects of LSD exhibit behavioral tolerance following chronic administration. The results suggest that behavioral tolerance after chronic LSD administration is incomplete, with tolerance exhibited to the acute impairment of habituation but potentiation of startle magnitude on both the first response and the first block of 30 trials. The Bleulerian concept of schizophrenia as a heterogeneous group of illnesses is emphasized. These results are interpreted as supporting the viability of LSD as a model for one or more of the group of schizophrenias. 17 references. (Author abstract modified)

001662 Brands, B.; Hirst, M.; Gowdey, C. W.; Baskerville, J. C. Dept. of Pharmacology, Health Sciences Centre, University of Western Ontario, London, Ontario, Canada **Analgesia duration and physical dependence in mice after a single injection of three heroin salts and morphine sulphate in various vehicles.** *Archives Internationales de Pharmacodynamie et de Therapie*. 231(2):285-296, 1978.

Analgesia duration and physical dependence following a single injection of three heroin salts and morphine sulphate in various vehicles were investigated in mice. Mice were given single subcutaneous injections of morphine sulphate (M.S.), heroin hydrochloride (H.HCl), and the sparingly soluble diheroin pamoate (H.PaM) and 3,5-di-tert-butyl-2,6-dihydroxybenzoate (H.Bnz) in three vehicles, saline, peanut oil, or a slow release vehicle and tested for analgesia by both the tail clip and potplate techniques. An inverse relationship was evident between the degree of dissociation of heroin from the three salts, at pH 7.3 and their durations of analgesia in vivo. The jumping behavior elicited by naloxone challenge was not consistently related to dose, salt form, or vehicle employed for the injection of agonists. The duration of analgesia observed and the intensity of the jumping response correlated significantly with the mean number of jumps per mouse after the naloxone challenge. 28 references. (Author abstract modified)

001663 Browne, Ronald G. Pfizer Inc., Pharmacology Research, Groton, CT 06340 **Effects of antidepressants and anticholinergics in a mouse European Journal of Pharmacology**. 58(3):331-334, 1979.

The specificity of the behavioral despair test (immobility during forced swimming) as a means of screening antidepressant drugs was examined in male CDI mice. Immobility was reduced not only by antidepressants, but also by drugs with anticholinergic properties, such as scopolamine, danitracin, benactyzine, benztropin, clozapine, and cyproheptadine. These findings indicate that the forced swimming/behavioral despair test is not selectively sensitive to antidepressants in mice. 5 references. (Author abstract modified)

001664 Browne, Ronald G.; Segal, David S. Segal: Psychiatry Dept. (M-003), School of Medicine, University of California, San Diego, La Jolla, CA 92093 **Behavioral activating effects of opiates and opioid peptides.** *Biological Psychiatry*. 15(1):77-86, 1980.

Locomotor activity of rats and mice was monitored following administration of the opiates, morphine, methadone, and etonitazene, or the opioid peptides, beta-endorphin, D-Ala2-Met5-enkephalinamide, and D-Met2-Pro5-enkephalinamide. In rats, these agents produced dose related biphasic patterns of activity consisting of an initial depression in locomotion followed by a period of hyperactivity. Intravenous administration of mor-

phine, methadone, or etonitazene in mice produced dose related increased in stereotyped locomotor activity. The metabolically resistant enkephalin analog, D-Met2-Pro5-enkephalinamide induced a similar pattern of effects. However, doses of beta-endorphin up to 20mg/kg, iv, failed to elicit locomotor stimulation in mice. The similarity in the naloxone reversible responses induced by opiates and certain opioid peptides suggests that the same underlying mechanisms may subserve their behavioral effects. 22 references. (Author abstract)

001665 Buccafusco, J. J.; Brezenoff, H. E. Brezenoff: Dept. of Pharmacology, CMDNJ-New Jersey Medical School, 100 Bergen Street, Newark, NJ 07103 **Opposing influences on behavior mediated by muscarinic and nicotinic receptors in the rat posterior hypothalamic nucleus.** Psychopharmacology. 67(3):249-254, 1980.

The opposing influences on behavior of muscarinic and nicotinic receptors in the rat posterior hypothalamic nucleus were examined. Microinjection of carbachol into the posterior hypothalamic nucleus (PHN) of freely moving rats evoked marked behavioral changes characterized by an escape reaction. This response was quantitated by measuring locomotor activity. In contrast, cholinergic stimulation of the PHN with neostigmine produced sedation and inactivity. Local pretreatment with the nicotinic receptor blocking agent mecamylamine blocked the excitatory effect of carbachol while the muscarinic antagonist atropine abolished the inhibitory effect of neostigmine on motor activity. It is concluded that behavioral changes evoked through cholinergic stimulation of the PHN may be mediated by a muscarinic system which controls sedation and a nicotinic pathway which mediates arousal. 27 references. (Author abstract modified)

001666 Burkhalter, John E.; Balster, Robert L. Balster: Box 613, MCV Station, Richmond, VA 23298 **Effects of phencyclidine on isolation-induced aggression in mice.** Psychological Reports. 45(2):571-576, 1979.

Mice isolated 6 to 8 weeks to induce aggression were injected with either saline, 1.0, or 3.0mg/kg phencyclidine (PCP), i.p. After 30 minutes, an untreated, group housed mouse (intruder) was introduced into the home cage of each isolated mouse (resident) for a 3 minute period. The frequency of resident mouse attack bite, tail rattles, nasal contacts, locomotions, and rearings was recorded by time sampling. The 1.0 PCP dose increased attack bites and decreased nasal contacts, while the 3.0mg/kg dose produced no change in these behaviors. Locomotions were increased at both PCP doses. Drug effects on agonistic and related behaviors are similar to the reported biphasic effects of d-amphetamine on aggression. 14 references. (Author abstract)

001667 Byrd, L. D. Yerkes Regional Primate Research Center, Emory University, Atlanta, GA 30322 **Magnitude and duration of the effects of cocaine on conditioned and adjunctive behaviors in the chimpanzee.** Journal of the Experimental Analysis of Behavior. 33(1):131-140, 1980.

The effects of cocaine were studied on two types of behavior, conditioned and adjunctive, in the chimpanzee and the time course of the effects of cocaine on these behaviors was investigated. Conditioned key-pressing was maintained under a multiple schedule of food presentation comprising fixed-interval and fixed-ratio components, and adjunctive drinking occurred in concert with the component schedules. Cocaine administered before a daily session increased responding during the fixed-interval component at doses that decreased drinking and had no effect on responding during the fixed-ratio components. A time course analysis showed the magnitude and duration of the effects of cocaine on key-pressing under the fixed-interval sched-

ule and on adjunctive drinking to be dose related. Moreover, it is reported that a given dose of cocaine had diverse effects, depending on the dose and the time since drug administration. 39 references. (Author abstract modified)

001668 Carter, C. J.; Pycoc, C. J. Dept. of Pharmacology, Medical School, CMDNJ-New Jersey Medical School, 100 Bristol BS8 1TD, England **The effects of 5,7-dihydroxytryptamine lesions of extrapyramidal and mesolimbic sites on spontaneous motor behaviour, and amphetamine-induced stereotypy.** Naunyn-Schmiedeberg's Archives of Pharmacology. 308(1):51-54, 1979.

Male Porton rats with 5,7-dihydroxytryptamine (5,7-DHT) lesion of the nucleus accumbens septi or substantia nigra showed a twofold increase in spontaneous locomotor activity, compared to vehicle injected controls. Striatal 5,7-DHT lesions also raised basal activity levels, as well as increasing rearing behavior in an open field. Stereotyped responses to 2.5 to 10mg/kg i.p. amphetamine were enhanced by lesions of the nucleus accumbens of substantia nigra, but striatal lesions affected only the response to the lowest dose. Lesions of the tuberculum olfactorium had no effect on spontaneous or amphetamine-induced responses. Results suggest that 5-hydroxytryptamine (5-HT) exerts a modulatory influence on nigrostriatal function and that 5-HT is antagonistic to dopamine function in the nucleus accumbens. 17 references. (Author abstract modified)

001669 Castellano, Claudio. Laboratorio di Psicobiologia e Psicofarmacologia, C.N.R., Via Reno, I-00198 Rome, Italy **Dose-dependent effects of heroin on memory in two inbred strains of mice.** Psychopharmacology. 67(3):235-239, 1980.

Heroin was administered to DBA/2 and C57BL/6 mice, trained in the five choice Yerkes/Thompson/Bryant/Bovet-Nitti apparatus for pattern discrimination, in two sets of experiments. In a first set, pretrial administrations of heroin (0.1, 0.25, or 0.5mg/kg) improved performance in both strains. In a second set, heroin (0.5mg/kg) immediately following each training session was followed by performance improvements in both strains, while the performance of C57 mice was improved and that of the DBA mice was impaired by 5mg/kg of opiate. No effect was evident in this set of experiments when heroin was injected 2 hours after each session, suggesting that effects of the pretrial treatments were due to influences of the opiate on the consolidation processes of the strains tested. 18 references. (Author abstract)

001670 Cheal, MaryLou. Neuropsychology Laboratory, McLean Hospital, Belmont, MA 02178 **Stimulus-elicited investigation in apomorphine-treated gerbils.** Behavioral and Neural Biology. 27(2):157-174, 1979.

The effects of the dopamine receptor stimulant, apomorphine hydrochloride (0.03 to 3.0mg/kg, subcutaneously), on stimulus elicited investigation were examined in Mongolian gerbils. The lowest dose of apomorphine did not significantly alter the duration or frequency of investigation of a novel object or odor source, but the highest dose severely decreased responding to either stimulus. After intermediate doses (1.0 or 2.0mg/kg), the duration but not frequency of investigatory behavior was decreased. The apomorphine effects were blocked by the dopamine antagonist pimozide. Results suggest that high doses of apomorphine activate postsynaptic dopamine receptors, whereas low doses stimulate presynaptic dopamine autoreceptors. 38 references. (Author abstract modified)

001671 Cheng, Richard S. S.; Pomeranz, Bruce Dept. of Zoology, University of Toronto, Toronto, Ontario, Canada M5S 1A1 **Electroacupuncture analgesia could be mediated by at least two pain-relieving mechanisms; endorphin and non-endorphin systems.** Life Sciences. 25(23):1957-1962, 1979.

The effects of naloxone and/or parachlorophenylalanine on electroacupuncture analgesia at high or low frequency stimulation were compared. Different levels of electroacupuncture analgesia were found to be induced by three different frequencies of stimulation (0.2, 4, and 200 Hz); highest analgesia was induced at 200 Hz and lowest at 0.2 Hz. Naloxone completely reversed the electroacupuncture effects at low frequency stimulation (4 Hz), but produced no inhibition at high frequency stimulation. Conversely, parachlorophenylalanine (320mg/kg) partially blocked the high frequency analgesia but produced no effect on the low frequency (4Hz) electroacupuncture analgesia. It is suggested that electroacupuncture analgesia induced by low frequency stimulation may be mediated by endorphins while high frequency stimulation is not endorphinergic but may be partly due to serotonin. 16 references. (Author abstract modified)

001672 Cherek, D. R.; Thompson, T.; Kelly, T. Dept. of Psychiatry, Louisiana State University Medical Center, P.O. Box 33932, Shreveport, LA 71130 **Chronic delta9-tetrahydrocannabinol administration and schedule-induced aggression.** *Pharmacology Biochemistry and Behavior*. 12(2):305-309, 1980.

The effects of 0.5mg/kg and 1.0mg/kg of delta9-tetrahydrocannabinol (delta9-THC) on keypecking maintained by a response initiated fixed-interval schedule of food presentation and schedule-induced aggression in the pigeon was studied. Initially, following the administration of delta9-THC both the rate of keypecking and attack responding were markedly reduced. Over sessions, tolerance developed to the suppressant effect on keypecking, with the rate returning to the predrug level. The suppressing effect of delta9-THC on the rate of attack remained at or near zero throughout the series of delta9-THC injections. It is concluded that the suppressant effect on schedule-induced aggressive behavior could represent an effect on schedule-induced or adjunctive behaviors as a class of behaviors rather than a specific effect on aggression. 30 references. (Author abstract modified)

001673 Chipkin, Richard E.; Stewart, John M.; Channabasaiah, K. Schering Corporation, 60 Orange Street, Bloomfield, NJ 07003 **The effects of peptides on the stimulus properties of ethanol.** *Pharmacology Biochemistry and Behavior*. 12(1):93-98, 1980.

The effects of peptides on the stimulus properties of ethanol were investigated with a discrimination training paradigm in rats. Male Sprague-Dawley rats were trained to discriminate ethanol from saline in a two bar positively reinforced operant task on a VI 15 second schedule. After the rats reached criterion performance (greater than 90% correct), thyrotropin releasing hormone (TRH), a metabolite of TRH (His-Pro diketopiperazine:HP), and a structural analog of TRH (HPCA-His-ThiaPro-NH₂:OHT) were tested for their ability to antagonize the ethanol cue. These peptides were chosen for their reported ability to reverse ethanol-induced narcosis. However, at doses that did not disrupt performance, TRH, HP, and OHT did not affect the stimulus properties of ethanol, nor did they change the stimulus properties of saline. Naloxone and ACTH(1-10)-NH₂ were also tested as ethanol antagonists of the training dose. Pretreatment with either of these compounds failed to alter ethanol appropriate responding. In addition, (DAla²-Met⁵)-enkephalin-ol, (DAla²-Met(O⁵)-enkephalin-ol, substance-P, delta sleep inducing peptide, and bombesin were tested for their ability to elicit ethanol appropriate responding. The ethanol cue generalized to none of these peptides. 31 references. (Author abstract modified)

001674 Clark, C. R.; Nowell, N. W. Department of Zoology, University of Hull, Hull, North Humberside, HU6 7RX, England **The effect of the antiestrogen CI-628 on androgen-induced aggressive behavior in castrated male mice.** *Hormones and Behavior*. 12(3):205-210, 1979.

The question of whether or not the antiestrogen CI-628 would block testosterone maintained fighting in castrated male mice was investigated. TO strain adult male mice were castrated and injected s.c. every day for 14 days with either: 1) 75mcg testosterone or 2) 75mcg testosterone and 1mg CI-628, and in addition, 1mg of CI-628 6 hours prior to each injection of antiestrogen and androgen. Vehicle injected, castrated, and CI-628 injected animals were employed as controls. Testosterone maintained intermale aggressive behavior was blocked by the antiestrogen CI-628. Support was obtained for the hypothesis that testosterone exerts its effects on the central nervous elements involved in the control of aggressive behavior by its aromatization to estrogenic metabolites. 22 references. (Author abstract modified)

001675 Collingridge, G. L.; Davies, J. School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Reversible effects of low doses of tetanus toxin on synaptic inhibition in the substantia nigra and turning behaviour in the rat.** *Brain Research*. 185(2):455-459, 1980.

Effects of small doses of tetanus toxin into the rat substantia nigra were examined. Doses 0.05 to 0.001 times the dose used in previous studies were found to induce an ipsilateral turning behavior and reduced, but did not abolish, synaptic inhibition in the substantia nigra; both effects were reversible. It is suggested that it is unlikely that the abolition of this or other synaptic inhibitions by much larger doses of tetanus toxin in earlier studies was a nonspecific effect. The mechanism previously proposed, viz, that tetanus toxin acted presynaptically by reducing the synaptic release of the transmitter, may account for the action of the toxin here reported. 20 references.

001676 Colpaert, Francis C.; Niemegeers, Carlos J. E.; Janssen, Paul A. J. Dept. of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **In vivo evidence of partial agonist activity exerted by purported 5-hydroxytryptamine antagonists.** *European Journal of Pharmacology*. 58(4):505-509, 1979.

Rats trained to discriminate 0.16mg/kg lysergic acid diethylamide (LSD) from saline showed partial generalization to cyproheptadine (1.25 to 10mg/kg), methysergide (0.16 and 10mg/kg), and mianserin (2.5 to 40mg/kg). The hallucinogens mescaline (5 to 40mg/kg) and quipazine (1.25 to 5mg/kg) were also generalized with LSD. Results suggest that cyproheptadine, methysergide, and mianserin may produce partial agonist effects in addition to their antagonistic action at central 5-hydroxytryptamine receptor sites. 12 references. (Author abstract modified)

001677 Contreras, E.; Tamayo, L.; Quijada, L. Dept. of Pharmacology, University of Concepcion, Concepcion, Chile **Effects of the irreversible inhibition of GABA transaminase upon some morphine effects.** *Neuropharmacology*. 18(3):309-313, 1979.

The effects of two irreversible inhibitors of GABA transaminase, gamma-acetylenic-GABA and gamma-vinyl-GABA, on the responses to morphine in female mice were examined. Both compounds intensified morphine analgesia, but large doses of gamma-acetylenic-GABA produced stimulant effects that masked a possible synergism. The potentiation of morphine's analgesic effects was greater in morphine tolerant animals than in naive mice. Both compounds attenuated physical dependence on morphine, except for high doses of gamma-acetylenic-GABA. Results suggest a relationship between some acute and chronic

effects of morphine and GABA concentration in the nervous system. 14 references. (Author abstract modified)

001678 Cooper, Steven J.; McClelland, Audrey. Dept. of Psychology, University of Birmingham, Birmingham B15 2TT, England **Effects of chlordiazepoxide, food familiarization, and prior shock experience on food choice in rats.** *Pharmacology Biochemistry and Behavior*. 12(1):23-28, 1980.

The effects of chlordiazepoxide, food familiarization, and prior shock experience on food choice in rats were studied. Chlordiazepoxide increased the time devoted to eating familiar laboratory chow without altering the response to a range of novel, palatable foods which were also available to the food deprived rats. Prior experience with the same range of alternative foods (food familiarization) radically changes the effect of the drug. After familiarization with these foods, chow was virtually ignored as a food choice, indicating its low relative palatability; chlordiazepoxide then prolonged the time eating the familiarized foods without significantly increasing the response to chow. These results are not consistent with an antidof neophobia action of chlordiazepoxide. They suggest instead that chlordiazepoxide enhances feeding responses related to food saliency. Footshock, delivered two days before the food choice test affected performance within the test. Its effects were opposite those of chlordiazepoxide, but they competed additively with the drug's effects. These results indicate that chlordiazepoxide's action is not simply to remove any inhibitory effect on feeding produced by fear; instead the drug promoted approach to food antagonizing any deficit in approach associated with fear. These findings are viewed as consistent with an action of chlordiazepoxide to augment the level of feeding motivation. Chlordiazepoxide may act to overcome food neophobia. 20 references. (Author abstract modified)

001679 Cusatis, Michele Ann. Southern Illinois University at Carbondale **Visual, olfactory and trigeminal loss: effects on amphetamine-induced stereotypy in the rat.** (Ph.D. dissertation). Dissertation Abstracts International. 40(8):4016-B, 1980. Ann Arbor, Univ. Microfilms No. 8004034, 88p. 1979.

Effects of sensory loss on amphetamine-induced stereotypy in the rat were investigated in a series of four experiments. In the first, the behavioral response to amphetamine of animals deprived of normal visual, olfactory, and trigeminal sensation was compared to that of a surgical control group. The remaining three studies provided an analysis of the effects of discrete manipulations in each modality in the absence of damage to the other two sensory systems. Data analysis indicated no systematic difference in the behavior of amphetamine treated rats as a result of the sensory manipulations. Possible theoretical and methodological shortcomings are considered and recommendations for further investigations are discussed. (Journal abstract modified)

001680 D'Mello, G. D.; Goldberg, D. M.; Goldberg, S. R.; Stolerman, I. P. MRC Neuropsychopharmacology Unit, Medical School, Birmingham B15 2TT, England **Conditioned taste aversion and operant behaviour in rats: effects of cocaine and a cocaine analogue (WIN 35,428).** *Neuropharmacology*. 18(12):1009-1010, 1979.

The effects of cocaine and Win-35,428, a long-acting cocaine analogue, on operant performance and conditioned taste aversion were compared in rats. In food deprived animals trained on a fixed ratio 30 schedule of food reinforcement, the doses needed to reduce the mean numbers of responses to 50% of the numbers after saline injection were 56mcml/kg for cocaine and 1.5mcml/kg for Win-35,428 (potency ratio, 37:1). Increasing the time between drug administration and testing in increments

from 5 minutes to 150 minutes showed that Win-35,428 had a slower onset of peak effect and about three times greater duration of action than cocaine. In conditioned taste aversion tests, the dose of Win-35,428 needed to produce a given degree of aversion was considerably lower than that of cocaine; 50% of the maximum possible degree of aversion was produced by 28mcml/kg cocaine or 0.83mcml/kg Win-35,428 in two flavor choice trials (potency ratio, 33:1). Results indicate that marked changes in duration of action do not necessarily have specific effect on potency in conditioned taste aversion. 6 references.

001681 Datta, P. C.; King, M. G. University of Newcastle, Newcastle, New South Wales 2308, Australia **Effects of MIF-I and melatonin on novelty-induced defecation and associated plasma 11-OHCS and brain catecholamines.** *Pharmacology Biochemistry and Behavior*. 11(2):173-181, 1979.

The effects of melanocyte stimulating hormone inhibiting factor-I (MIF-I) and of melatonin on step down latencies, defecation, plasma 11-hydroxycorticosterone (11-OHCS), and whole brain dopamine (DA) and norepinephrine (NE) concentration were examined in two experiments involving 5 days' novelty exposure. Treatment with MIF-I led to a significant habituation of novelty-induced defecation over 5 days, whereas plasma 11-OHCS was reduced only on day 1. Concentrations of whole brain DA and NE showed a significant increase over days of MIF-I and novelty treatment. Melatonin treatment significantly inhibited defecation and reduced plasma 11-OHCS level on day 5 of novelty exposure. Melatonin treatment led to a significant increase of whole brain DA in animals exposed to novelty for 5 days. Neither MIF-I nor melatonin significantly affected step down activity of treated rats. Overall, results suggest a possible relationship between novelty-induced defecation and brain DA levels of MIF-I and melatonin treated animals. 42 references. (Author abstract)

001682 Davis, Hasker P.; Rosenzweig, Mark R.; Bennett, Edward L.; Squire, Larry R. Dept. of Psychology, University of California, Berkeley, CA **Inhibition of cerebral protein synthesis: dissociation of nonspecific effects and amnesic effects.** *Behavioral and Neural Biology*. 28(1):99-104, 1980.

Mice were injected with 210mg/kg of anisomycin 5 hours prior to training and this produced more nonspecific behavioral side-effects at the time of training than did low dosage (30mg/kg) given 20 minutes prior to training. Yet the low dosage 20 minutes pretraining produced greater protein synthesis inhibition at training and greater impairment of retention of passive avoidance training than did the high dosage 5 hours pretraining. These results demonstrate that the level of protein synthesis inhibition at or near the time of training is the critical factor for inducing amnesia, and not nonspecific side-effects of a protein synthesis inhibiting drug. Various alternative hypotheses would also predict greater amnesia after the high dosage of anisomycin given 5 hours prior to training than after the amnesic low dose given 20 minutes prior to training. These results provide further support for the hypothesis that brain protein synthesis is required for long-term memory formation. 10 references. (Author abstract)

001683 Davis, N.; LeVere, T. E. Neuropsychology Laboratory, Dept. of Psychology, North Carolina State University, Raleigh, NC 27650 **Recovery of function after brain damage: different processes and the facilitation of one.** *Physiological Psychology*. 7(3):233-240, 1979.

The role of learning in recovery of function after brain damage was studied. All of the experiments involved hooded rats trained in a two choice brightness discrimination when treated with the RNA antimetabolite 8-azaguanine. The effects

of 8-azaguanine on the recovery of a preoperatively acquired brightness discrimination following posterior decortication were examined. The prediction was that if learning was involved in the recovery process, then recovery under the influence of 8-azaguanine should be impaired. However, the recovery process was actually facilitated when the animals were treated with 8-azaguanine. Another experiment tested whether the facilitation was some general facilitation of recovery of function or specifically related to the disruption of learning by 8-azaguanine. The drug 8-azaguanine impaired recovery of function. On the basis of these data, it is suggested that postoperative learning can interfere retroactively with the reinstatement of spared neural mechanisms when these neural mechanisms are effective in the recovery process. 14 references. (Author abstract modified)

001684 Davis, Paula G.; Chaptal, Claude V.; McEwen, Bruce S. Rockefeller University, New York, NY 10021 **Independence of the differentiation of masculine and feminine sexual behavior in rats.** *Hormones and Behavior*. 12(1):12-19, 1979.

To provide a more complete profile of the developmental effects of neonatal 1,4,6-androstatriene-3,17-dione (ATD) treatment on the sexual behavior of male rats, three issues were addressed: defeminization, masculinization, and sexual preference. Male rats received Silastic implants of ATD on days 2 to 10 of life. Controls received blank implants. There were no differences in the masculine sexual behavior of ATD and control males when tested as gonadally intact adults. During a sexual preference test, in which access was provided to both a sexually receptive female and to a stud male, there was no difference in the proportions of ATD and control males that copulated with the stimulus female. All animals were then castrated and tested twice for feminine sexual behavior under exogenous estradiol benzoate and progesterone. Results indicate that the propensity of males to show feminine sexual behavior can be manipulated independently of the capacity for masculine sexual behavior. Results also suggest that the process of defeminization may occur primarily postnatally in rats since treatment during that period results in substantial increments in later feminine sexual behavior including solicitation behaviors. 12 references. (Author abstract modified)

001685 de Lanerolle, N. C.; Millam, J. R. Section of Neurological Surgery, Room 226 LSO, Yale University Medical School, 310 Cedar Street, New Haven, CT 06510 **Dopamine, chick behavior, and states of attention.** *Journal of Comparative and Physiological Psychology*. 94(2):346-352, 1980.

The behavioral effects of apomorphine hydrochloride on normal 5-day-old domestic chicks and on chicks pretreated with pimozide or haloperidol were studied. Five classes of relations between chick behavior and the drugs were observed. Apomorphine increased locomotion, and pecks at conspicuous objects were antagonized by pimozide and haloperidol. Apomorphine-induced decreases in the number of comfort movements and the duration of immobility were completely antagonized by pimozide and haloperidol, whereas the reduction in the duration of eye closure was only partially reversed. Pimozide and haloperidol by themselves decreased locomotion, comfort movements, pecks at the bird's own legs, and total number of pecks observed, and each increased the duration of eye closure. Head shakes, body shakes, and pecks at the bird's own legs were increased by apomorphine only in pimozide and haloperidol pretreated birds. In the dark, apomorphine induced very few trills, but twitters were increased. It is argued that many of the behavioral changes induced by the above drugs may be caused through dopamine dependent mechanisms and that the changes in behavior are the consequence of a primary change in the bird's attention to stimuli. 17 references. (Author abstract modified)

001686 Delini-Stula, A.; Baumann, P.; Buch, O. CIBA-Geigy AG Basel, Research Dept., Pharmaceuticals Division, CH-4002 Basel, Switzerland **Depression of exploratory activity by clonidine in rats as a model for the detection of relative pre- and postsynaptic central noradrenergic receptor selectivity of alpha-adrenolytic drugs.** *Naunyn-Schmiedeberg's Archives of Pharmacology*. 307(2):115-122, 1979.

The effects of alpha-adrenoceptor blocking drugs on the depression of exploratory activity induced by 0.1mg/kg i.p. clonidine in male Tif:RAif rats and on presynaptic and postsynaptic alpha-receptors in field stimulated cortex slices and isolated vas deferens were examined. Tolazoline, esproquine, yohimbine, and piperoxan antagonized the depressant effects of clonidine on exploration and showed preferential action on presynaptic alpha-receptors. Phenolamine and phenoxybenzamine showed preferential blocking activity on postsynaptic alpha-receptors and potentiated rather than antagonized the behavioral effects of clonidine. Mianserin preferentially blocked postsynaptic receptors but had no effect on clonidine-induced hypoactivity. The antagonism of clonidine by the selective presynaptic alpha-receptor blockers was observed within a limited dose range, possibly reflecting a counterbalancing postsynaptic blockade at higher dosages. Results revealed a good correlation between antagonism of clonidine in vivo and preferential blockade of presynaptic alpha-receptors in vitro. 38 references. (Author abstract modified)

001687 Delini-Stula, Alexandra; Vassout, Annick. Research Dept., Pharmaceuticals Division, Ciba-Geigy Ltd., Basel, Switzerland **Modulation of dopamine-mediated behavioural responses by antidepressants: effects of single and repeated treatment.** *European Journal of Pharmacology*. 58(4):443-451, 1979.

The effects of maprotiline, imipramine, clomipramine, and amitriptyline on the stereotyped and turning behavior induced by apomorphine in male Tif:RAif rats were examined. Single or repeated doses of maprotiline or imipramine (25mg/kg i.p.) failed to alter stereotyped responses to apomorphine. In contrast, clomipramine showed an inhibitory effect which increased after 7 daily injections of the drug. Repeated doses of amitriptyline also produced a moderate suppression of apomorphine-induced stereotypies. In rats with unilateral 6-hydroxydopamine lesions of the substantia nigra, apomorphine-induced contralateral turning was markedly suppressed (70%) after a single 25mg/kg injection of maprotiline, but tolerance to this effect developed after 7 daily injections. Clomipramine and amitriptyline inhibited turning, and this effect increased markedly with repeated treatment. Results indicate that antidepressants do not uniformly affect behavioral responses mediated by dopamine. 41 references. (Author abstract modified)

001688 Della-Fera, Mary Anne; Baile, Clifton A.; McLaughlin, Carol L. Dept. of Clinical Studies at New Bolton Center, School of Veterinary Medicine, University of Pennsylvania, Kennett Square, PA 19348 **Feeding elicited by benzodiazepine-like chemicals in puppies and cats: structure-activity relationships.** *Pharmacology Biochemistry and Behavior*. 12(2):195-200, 1980.

To assess the relationship between the structure of benzodiazepines and their activity as feed intake stimulants, benzodiazepines of different structural subclasses were given per os as a drench to puppies and young cats. The chemicals included diazepam (D), elfazepam (E), a 1,5 benzodiazepine (WE405), a triazolobenzodiazepine (U31889), a 1-pyridyl triazolobenzodiazepine (U37576), and a thienotriazolodiazepine (WE941). In puppies, U37576 was the most potent chemical, while E elicited greater feeding responses. In cats, E also stimulated the most feeding, but WE941 and U31889 were the most potent chemicals. WE405 was the least effective chemical in puppies but worked

well as a stimulant of 24 hour feed intake in cats. The cats were two to seven times more sensitive than the dogs to the effects of chemicals. All the chemicals except E caused some degree of either ataxia or excitement in both puppies and cats. E is proposed to be most useful therapeutically as an oral feed intake stimulant for these species. 28 references. (Author abstract modified)

001689 Domjan, Michael; Gillan, Douglas J.; Gemberling, Gail A. Dept. of Psychology, Mezes 330, University of Texas, Austin, TX 78712 **Aftereffects of lithium-conditioned stimuli on consummatory behavior in the presence or absence of the drug.** *Journal of Experimental Psychology: Animal Behavior Processes*. 6(1):49-64, 1980.

The aftereffects of lithium conditioned stimuli on consummatory behavior in the rat were examined in a series of experiments. Drinking was increased by prior exposure to lithium conditioned stimuli. Experiment 1 showed that this phenomenon is not an artifact of testing subjects with a novel, palatable drinking fluid and also showed that lithium conditioned olfactory stimuli produce a biphasic change in drinking, with drinking suppressed at the start of exposure to the conditioned stimulus (CS) and enhanced a long time after CS onset or exposure. Experiment 2 showed that the increased drinking aftereffect of lithium conditioned stimuli is not a result of the instrumental reinforcement of the drinking response by the scheduling of water access following drug injections during conditioning. Experiments 3, 4, and 5 showed that the increased drinking effect occurs even if subjects are injected with lithium prior to the test session. The results also showed that lithium administration and exposure to lithium conditioned stimuli have independent and opposite aftereffects. Lithium disrupts drinking, whereas prior exposure to lithium conditioned stimuli increases consumption. The relevance of conditioned opponent and compensatory processes to the findings is discussed. 35 references. (Author abstract modified)

001690 Downs, David A.; Miller, Larry E.; Wiley, James N.; Johnston, Donald E. Warner-Lambert/Parke-Davis Pharmaceutical Research Division, Dept. of Pharmacology, 2800 Plymouth Road, Ann Arbor, MI 48105 **Oral vs. parenteral drug effects on schedule-controlled behavior in rhesus monkeys.** *Life Sciences*. 26(14):1163-1168, 1980.

The effects of various drugs administered by different routes on schedule controlled behavior in rhesus monkeys were compared. Intramuscular, intravenous, and subcutaneous injections of heroin, methadone, morphine, LAAM, cocaine, d-amphetamine, and phencyclidine produced about equivalent effects on schedule controlled responding. By the buccal route, potency was reduced by approximately three fold except with cocaine and heroine; with cocaine, buccal potency was equivalent to the parenteral routes while with heroine, buccal potency was reduced by about 20 fold. By the oral route, methadone, morphine, heroin, and phencyclidine were at least 50 to 100 times less potent than by i.m., i.v., or s.c. routes. It is concluded that for certain drugs like methadone and phencyclidine, relative potencies by oral vs. parenteral routes in rhesus monkeys differ greatly from those obtained in humans. 15 references. (Author abstract modified)

001691 Drust, Eugene G.; Sloviter, Robert S.; Connor, John D. Dept. of Pharmacology, Milton S. Hershey Medical Center, Pennsylvania State University College of Medicine, Hershey, PA 17033 **Effect of morphine on cerebroventricular injection of serotonin.** *Pharmacology*. 18(6):299-305, 1979.

Intraventricular administration of serotonin (5-HT) to male Sprague-Dawley rats caused wet dog shakes, a sign of morphine

withdrawal. The frequency of shakes was dose dependent. Shaking was potentiated by pretreatment with a monoamine oxidase inhibitor or with 5,7-dihydroxytryptamine and was depressed by morphine or 5-HT receptor blockers. Naloxone rapidly reversed the inhibition of 5-HT shaking induced by morphine, but not the inhibition induced by 5-HT receptor blockers. 25 references. (Author abstract modified)

001692 Duteil, Jacques; Rambert, Francis A.; Pessonnier, Jeanne; Gombert, Roger; Assous, Emile. Centre de Recherches du Laboratoire L. Lafon, 1, Rue Georges Mederic, F-94701 Maisons-Alfort, France **A possible alpha-adrenergic mechanism for drug (CRL 40028)-induced hyperactivity.** *European Journal of Pharmacology*. 59(1/2):121-123, 1979.

The mechanisms by which benzhydryl sulfinyl acetohydroxamic acid (CRL 40028) stimulates locomotor activity was studied in male NMRI mice. Phenoxybenzamine (20mg/kg i.p.), prozac (0.5 to 1mg/kg i.p.), and yohimbine (2mg/kg i.p.) prevented the development of CRL-40028 induced hyperactivity. Results suggest that stimulation of an alpha-adrenergic postsynaptic receptor is involved in the stimulant effect of CRL-40028. 10 references. (Author abstract modified)

001693 Earley, C. J.; Leonard, B. E. Department of Pharmacology, University College, Galway, Ireland **Effects of prior exposure on conditioned taste aversion in the rat: androgen- and estrogen-dependent events.** *Journal of Comparative and Physiological Psychology*. 93(5):793-805, 1979.

The effects of preexposure and gonadal hormone manipulation on the extinction of a conditioned taste aversion in rats were investigated. In Experiment 1, male rats were given one prior exposure to sucrose at some selected time before a second exposure to sucrose and an LiCl injection. Under the single exposure condition, castrated animals extinguished the aversion faster than either testosterone treated castrated rats or sham operated rats. In Experiment 2, estradiol, dihydrotestosterone, and testosterone were studied by using only a Day 1 preexposure condition. The testosterone treated group maintained the aversion for the longest period of time, followed by dihydrotestosterone treated, sham, castrated, and estradiol treated groups. It appears that estradiol augments the castration effect whereas dihydrotestosterone attenuates the effect. In Experiment 3, estradiol was administered alone or in combination with two different doses of dihydrotestosterone, and a Day 1 preexposure condition was used. The findings indicate that the outcome of behavior is dependent on the ratio of estradiol to dihydrotestosterone, with variations in this ratio resulting in fast (estrogen effect) to slow (androgen effect) rates of extinction. 27 references. (Author abstract modified)

001694 Eichler, Alan J.; Antelman, Seymour M. Psychobiology Program, Dept. of Psychology, University of Pittsburgh, Pittsburgh, PA 15260 **Sensitization to amphetamine and stress may involve nucleus accumbens and medial frontal cortex.** *Brain Research*. 176(2):412-416, 1979.

The interaction of self-stimulation (SS) stress and d-amphetamine (AM) was examined in male Sprague-Dawley rats with electrodes implanted in sites associated with the mesolimbic dopamine projection (nucleus accumbens, NA), mesocortical dopamine pathway (medial frontal cortex, MFC), or nigrostriatal dopamine pathway (A-9 nucleus). Animals were tested for stereotypy and anorexia in response to 2mg/kg i.p. AM 24 hours after cessation of 4 to 7 weeks of daily 0.5 hour SS sessions. Chronic SS in the NA and MFC significantly enhanced AM stereotypy and anorexia, but chronic A-9 SS had no effect. Drinking behavior was also enhanced in animals that had been self-stimulating in the MFC, and this response displayed sensitization over

time. The NA SS animals showed enhanced eating, but no sensitization to this response was observed. Ingestive behavior did not differ from controls in the A-9 SS animals. These findings indicate that repeated stress can produce sensitization to AM as well as to subsequent stress and that the mesocortical dopamine projection is involved in the sensitization phenomena. These findings also suggest that AM psychosis may reflect sensitization to stress. 21 references.

001695 Elisabetsky, Elaine; Vendite, Deusa A.; Izquierdo, Ivan. Departamento de Bioquímica, Instituto de Biociências, UFRGS, 9000 Porto Alegre, RS, Brazil **Memory channels in the rat: effect of post-training application of potassium chloride on the hippocampus.** *Behavioral and Neural Biology.* 27(3):354-361, 1979.

To examine memory channels in the rat, Ss were trained to perform shuttle responses to a buzzer either in a Pavlovian paradigm or an avoidance situation without stimulus pairing. Seven days later, Ss were tested either in the same paradigm in which they had been trained or in the other one. Evidence was obtained for retention in all groups and it involved both direct and transfer memory. The two memory transfers were enhanced in Ss who received an application of potassium chloride to the dorsal hippocampus immediately after training. Control groups were either intact animals or rats with bilateral hippocampal cannulas. The data support the concept of separate and parallel memory channels in the rat brain. 28 references. (Author abstract modified)

001696 Ellison, Gaylord; Ring, Michael; Ross, Davis; Axelrod, Bryant. Dept. of Psychology, University of California, Los Angeles, CA 90024 **Cumulative alterations in rat behavior during continuous administration of LSD or mescaline: absence of tolerance?** *Biological Psychiatry.* 15(1):95-102, 1980.

Male hooded rats were observed for 6 days following implantation with slow release subcutaneous pellets containing LSD, mescaline, or control vehicle solution. In animals housed in isolation cages, continuous hallucinogen administration resulted in a gradual increase in head twitches and catatonic postures which peaked 3 to 4 days after pellet implantation and then declined. In animals housed in social colonies, there were also delayed increases in behavior following hallucinogen pellet implantation, but these principally involved social behaviors such as fighting by mescaline treated animals and social grooming by LSD treated animals. This finding of gradual and cumulative effects of continuous hallucinogen administration contrasts with the usual finding of a rapid tolerance to hallucinogens following repeated injections. 15 references. (Author abstract)

001697 Etgen, Anne M.; Whalen, Richard E. Department of Biology, Livingston College, Rutgers University, New Brunswick, NJ 08903 **Masculinization and defeminization induced in female hamsters by neonatal treatment with estradiol, RU-2858, and nafoxidine.** *Hormones and Behavior.* 12(3):211-217, 1979.

The effects of the antiestrogen nafoxidine on the development of the potential to show masculine and feminine sexual behavior in adulthood was studied with newborn hamsters. Newborn female hamsters were treated with 0.1ng or 1.0ng of estradiol benzoate (EB), with 1.0ng to 2.0mcg of the synthetic estrogen RU-2858, or with 0.1 or 0.5mcg of nafoxidine. When adult the animals were treated with EB and progesterone and tested for the display of lordosis and treated with testosterone propionate and tested for the display of mounting behavior. The EB doses used failed to alter sexual differentiation. RU-2858 masculinized and defeminized in a dose dependent manner being most effective when given neonatally as two divided doses. Nafoxidine inhibited lordosis without enhancing mounting behavior. The findings support the hypothesis that estrogens may be involved

in the normal sexual differentiation process. 6 references. (Author abstract modified)

001698 Fanselow, Michael S.; Bolles, Robert C. Dept. of Psychology, University of Washington, Seattle, WA 98195 **Naloxone and shock-elicited freezing in the rat.** *Journal of Comparative and Physiological Psychology.* 93(4):736-744, 1979.

Effects of naloxone on shock elicited freezing was studied in the rat. Freezing behavior following painful electric shock was found to increase following pretreatment with the opiate antagonist, naloxone. Freezing was a positive linear function of drug dose and shock intensity. Naloxone pretreatment enhanced freezing only when the animal received two or three shocks, but not when the animal received only one shock or no shock. Naloxone must be present during shock, not just during the observation period, in order to increase freezing. Results suggest that when an animal is shocked, endorphins are released which make subsequent shocks less aversive. Naloxone, by blocking the endorphin system, makes the shock more aversive than it would normally be. 23 references. (Author abstract modified)

001699 Feldon, J.; Guillaumon, A.; Gray, Jeffrey A.; De Wit, H.; McNaughton, N. Gray: Department of Experimental Psychology, University of Oxford, South Parks Road, Oxford OX1 3UD, England **Sodium amobarbitone and responses to nonreward.** *Quarterly Journal of Experimental Psychology.* 31(Part 1):19-50, 1979.

Three experiments are reported testing two alternative hypotheses concerning the behavioral effects of sodium amobarbitone (SA): 1) that it blocks the aftereffect of nonreward; 2) that it blocks conditioned frustration, elicited by stimuli associated with nonreward. In support of the second hypothesis, Experiment 1 shows that SA given in acquisition abolished the partial reinforcement extinction effect (PREE) when rats were run at one trial a day in an alley for food reward on a continuous (CRF) or partial (PRF) reinforcement schedule. Experiment 2 shows that, in the goal section, the effect of the drug on the PREE was due to its presence during acquisition and was not due to state dependency of the PREE. In Experiment 3, which supports the results of the second experiment, SA given to rats trained to show patterned running for water reward on a single alternation schedule blocked patterning by increasing running speeds on nonreward trials, not by decreasing running speeds on rewarded trials. 48 references. (Author abstract modified)

001700 Ferko, Andrew P.; Bobyock, Emil; Chernick, Warren S. Dept. of Pharmacology, Hahnemann Medical College and Hospital, Philadelphia, PA 19102 **A study on diazepam and postwithdrawal drinking of ethanol solution in rats.** *Toxicology and Applied Pharmacology.* 50(2):355-363, 1979.

The effects of diazepam on postwithdrawal drinking of ethanol solution were examined in Sprague-Dawley rats. A 10 day ethanol inhalation procedure was used to produce physical dependence on ethanol; signs of withdrawal were manifested in all ethanol treated animals but not in control animals. Each group of animals was divided into two groups, one for diazepam administration and one for vehicle the free choice drinking study indicate that diazepam did not enhance ethanol consumption in animals which were physically dependent on ethanol, but significantly suppressed ethanol drinking in nondependent animals. When examining the effect of physical dependence alone on postwithdrawal drinking, it appeared that no increase in ethanol preference was observed with animals under the experimental design. 28 references. (Author abstract modified)

001701 File, Sandra E.; Hyde, J. R. G.; Macleod, N. K. Dept. of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Sq., London, WC1N 1AX, England **5,7-dihy-**

droxytryptamine lesions of dorsal and median raphe nuclei and performance in the social interaction test of anxiety and in a home-cage aggression test. *Journal of Affective Disorders*. 1(2):115-122, 1979.

In order to determine whether adrenocorticotrophic hormone (ACTH) acts on midbrain 5-HT pathways, the effects of injected ACTH were examined in dorsal raphe nuclei and median raphe nuclei lesioned rats. Within each lesion group, rats were randomly allocated to three test conditions: low light, familiar; low light, unfamiliar; and high light, unfamiliar. Pairs of rats were placed in the center of a test arena and observed for 10 minutes on a video screen, with behaviors scored as social interaction. Five days after this test, rats were given the home cage intruder test, in which an unoperated intruder rat was introduced into the experimental rat's cage. Interactions were scored for 5 minutes. Results show that injections of ACTH 1-24 (corticotrophin) significantly reduced the active social interactions in control rats and rats with lesions of the median raphe nucleus, while not affecting the rats with lesions of the dorsal raphe nucleus. Dorsal raphe lesioned rats showed significantly fewer interactions of all kinds when an intruder rat was placed in their home cages. 19 references. (Author abstract modified)

001702 Fitzpatrick, D.; Halote, B. A.; Stohlman, J. M. Dept. of Psychology, California State University, 5151 State University Dr., Los Angeles, CA 90032 **Effects of neonatal administration of clomiphene citrate on sexual behavior of female rats: a preliminary report.** *Perceptual and Motor Skills*. 50(1):211-216, 1980.

The effects of neonatal administration of clomiphene citrate on sexual behavior of female rats were examined. Analysis showed that treatment with clomiphene for the first 5 days post-partum completely disrupted the adult sexual behavior of the female. In 5 consecutive days of testing the experimental females were never observed to mate. They were mounted less often than controls, suggesting that the males were less attracted to them than to normal females. It is concluded that the initial suggestion that clomiphene might affect the sexual behavior of female rats is supported; however, further research must be done to identify the underlying mechanism of the change. 20 references. (Author abstract modified)

001703 Flaherty, Charles F.; Lombardi, Bruce R.; Wrightson, John; Deptula, Dennis. Dept. of Psychology, Busch Campus, Rutgers University, New Brunswick, NJ 08903 **Conditions under which chlorthalidone influences gustatory contrast.** *Psychopharmacology*. 67(3):269-277, 1980.

Conditions under which chlorthalidone (CDP) influences gustatory contrast were investigated. Rats shifted from 32% sucrose to 4% sucrose consumed less 4% sucrose than animals without prior experience with 32% sucrose. The influence of CDP on this successive negative contrast obtained in sucrose ingestion was investigated in four experiments. Results indicate that: 1) rats injected with CDP during both preshift experience with 32% sucrose and postshift experience with 4% sucrose showed an essentially unchanged contrast effect compared with saline injected rats; 2) CDP injection for the first time on postshift day 2 eliminated contrast but postshift day 1 injections had little effect; 3) animals injected with CDP throughout preshift and switched to saline coincident with the sucrose shift showed a contrast effect at least as great as control animals, and 4) injections of CDP tended to elevate lick rate regardless of other conditions. These results indicate a disinhibitory effect of CDP and possible neophobia operating on the first postshift day. 39 references. (Author abstract modified)

001704 Flaherty, Charles F.; Meinrath, Anne B. Rutgers University, New Brunswick, NJ 08903 **The influence of scopolamine**

on sucrose intake under absolute and relative test conditions. *Physiological Psychology*. 7(4):412-418, 1979.

The influence of scopolamine on sucrose intake under absolute and relative test conditions was investigated in three experiments. Rats were injected with either saline or scopolamine hydrobromide in both simultaneous and successive contrast paradigms involving shifts between 32% and 4% sucrose solutions. One experiment included methyl scopolamine nitrate as a control for peripheral effects of the drug. Neither scopolamine hydrobromide nor methyl scopolamine nitrate had a clear cut disinhibitory effect on the occurrence of negative contrast. Instead, scopolamine hydrobromide reduced intake of the sucrose solutions, particularly the 4% solution, both preshift and postshift. 30 references. (Author abstract modified)

001705 Ford, K. E.; Fowler, S. C.; Nail, G. L. Dept. of Psychology, University of Mississippi, University, MS 38677 **Effects of clozapine and chlorpromazine upon operant response measures in rats.** *Pharmacology Biochemistry and Behavior*. 11(2):239-241, 1979.

The effects of oral chlorpromazine (1, 3, 9mg/kg) and clozapine (2.5, 5, 10mg/kg) on intensive measures of response (peak force and duration) and rate were examined in rats under FR20 schedules of reinforcement with either a low or a high force requirement for reinforcer delivery. Conjoint examination of the three dependent variables revealed that clozapine affected FR responding in the same way as chlorpromazine. More specifically, response rate and peak force declined as a function of dose for each drug. Duration of response tended to be increased at the highest dose for both clozapine and chlorpromazine, but this effect was limited primarily to the high force condition. 15 references. (Author abstract modified)

001706 Foye, William O.; Tovivich, Suchinta. Samuel M. Best Research Laboratory, Massachusetts College of Pharmacy, Boston, MA 02115 **Heterocyclic analogs of amphetamine: thioureas, dithiocarbamates, and negatively substituted amides.** *Journal of Pharmaceutical Sciences*. 68(5):591-595, 1979.

A series of heterocyclic analogs of amphetamine was synthesized. The heterocycles used included the 2-furyl, 2-thienyl, 3-methyl-2-thienyl, 3-pyridyl, and 6-methyl-2-pyridyl rings. The aliphatic amine group was converted to the N-methylthiourea, dithiocarbamate, methanesulfonyl, trifluoromethanesulfonyl, and trifluoroacetyl fractions. The 2-thienyl analog of amphetamine produced a behavior pattern in rats similar to that seen after amphetamine, whereas the dithiocarbamate of the 6-methyl-2-pyridyl analog showed behavioral effects. The methylthiourea of the p-chloro analog also showed many behavioral effects of amphetamine; the methanesulfonamide and dithiocarbamate showed fewer of these effects. Antiarthritic, antimicrobial, and passive cutaneous anaphylactic effects were also observed with some compounds. The 3-methyl-2-thienyl analog of amphetamine significantly increased papillary muscle contractile force without producing arrhythmias. 15 references. (Author abstract modified)

001707 Fozard, J. R.; Palfreyman, M. G. Centre de Recherche Merrell International, 16, Rue d'Ankara, F-67084 Strasbourg Cedex, France **Metoclopramide antagonism of 5-hydroxytryptophan-induced Naunyn-Schmiedeberg's Archives of Pharmacology.** 307(2):135-142, 1979.

The effects of metoclopramide, methysergide, and haloperidol on wet dog shakes (WDS) induced in male Sprague-Dawley rats by injections of 5-hydroxytryptophan (5-HTP) were examined. All three drugs inhibited the 5-HTP-induced WDS. Methysergide appeared to act by blocking postsynaptic receptor sites for 5-hydroxytryptamine (5-HT). Metoclopramide and haloperi-

dol, however, caused catalepsy at doses that inhibited WDS, suggesting these compounds inhibited WDS by blocking dopamine receptors and inhibiting the ability to initiate movement. Since agents with cataleptic properties, probably unconnected to brain 5-HT mechanisms, are effective antagonists of the WDS response to 5-HTP, this model may not be an appropriate screen for drugs interacting with 5-HT receptors. 31 references. (Author abstract modified)

001708 Frances, H.; Lecrubier, Y.; Puech, A. J.; Simon, P. Simon: Departement de Pharmacologie, Faculte de Medecine Pitie-Salpetriere, 91, boulevard de l'Hopital, F-75634 Paris Cedex 13, France **Evidence for the role of noradrenaline in some effects of quipazine.** *Psychopharmacology*. 67(3):307-310, 1980.

Evidence for the role of noradrenaline in some effects of quipazine is presented and discussed. In mice, quipazine has shown several behavioral effects: it antagonizes hypothermia induced by a high dose of apomorphine without altering climbing or stereotyped behavior; it antagonizes oxotremorine-induced hypothermia without altering tremors or peripheral signs; and it increases the toxicity of yohimbine. These three responses are considered to be predictive of an antidepressant action; in these three tests the effects of quipazine are inhibited by D,L-propranolol but not by D-propranolol or methysergide. Quipazine, in mice pretreated with pargyline, induced head twitches which were inhibited by methysergide but not by D,L-propranolol. Quipazine, in addition to its well known serotonergic effects, seems to have beta adrenergic properties which should be kept in mind when this drug is used as a pharmacological tool and which suggest that the beta-adrenergic system is implied in depression. 16 references. (Author abstract modified)

001709 Freed, William J.; Gillin, J. Christian; Wyatt, Richard J. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Anticonvulsant properties of betaine.** *Epilepsia*. 20(3):209-213, 1979.

Determining whether betaine blocks only those convulsions induced by homocysteine or, conversely, whether betaine has more general anticonvulsant properties was investigated. Results indicate that betaine was found to block the induction of convulsions by electroconvulsive shock and by pentylenetetrazol at least as effectively as it blocked convulsions induced by homocysteine. It is concluded that betaine has a general anticonvulsant action, the reason for which is unknown. 15 references. (Author abstract modified)

001710 Freed, William J.; Gillin, J. Christian; Wyatt, Richard J. Laboratory of Clinical Psychopharmacology, Div. of Special Mental Health Research, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Anomalous behavioral response to imidazoleacetic acid, a GABA agonist, in animals treated chronically with haloperidol.** *Biological Psychiatry*. 15(1):21-35, 1980.

The paradoxical phenomenon that short-term haloperidol treatment decreases the stimulant effect of drugs with dopamine-like action, while withdrawal from long-term haloperidol treatment enhances the effects of such drugs, was investigated. It is demonstrated that withdrawal from long-term haloperidol treatment decreases or eliminates the tendency for imidazole-4-acetic acid, a GABA agonist, to decrease the locomotor activity of mice. Acute haloperidol treatment did not duplicate these effects. It is suggested that chronic administration of haloperidol causes changes in a variety of systems in the brain, and that the GABA system in particular is profoundly altered by such treatment. 37 references. (Author abstract modified)

001711 Frey, H.-H.; Loscher, W. Laboratory of Pharmacology and Toxicology, School of Veterinary Medicine, Free University, Berlin, Germany **Cetyl GABA: effect on convulsant thresholds**

in mice and acute toxicity. *Neuropharmacology*. 19(2):217-220, 1980.

In mice, the intraperitoneal injection of the cetyl ester of GABA in doses of 10 to 25mg/kg provoked significant increases in the thresholds for the maximal electroconvulsion and the clonic component of the pentetrazole convulsion. At the same time the GABA levels in brain were elevated by 7% to 25%. To obtain comparable effects, doses of 2g/kg of GABA had to be administered. At a dose of 100mg/kg of cetyl GABA, the convulsant thresholds were also increased after oral administration. There was no protection against convulsions elicited by the subcutaneous injection of 100mg/kg of pentetrazole. Cetyl GABA was fairly toxic by the intravenous and intraperitoneal routes, but was well tolerated when given orally. 20 references. (Author abstract)

001712 Funk, Klaus F.; Westermann, K. H. Institute of Pharmacology and Toxicology, Medical Academy **Dopaminergic pathways in the rat central nervous system and rotational behaviour.** *Pharmacology Biochemistry and Behavior*. 11(2):135-139, 1979.

The effects of lesions of the substantia nigra (SN), area ventralis tegmenti (AVT), or globus pallidus (GP) on rotational behavior were examined in the rat. Unilateral lesion of the SN or AVT caused ipsilateral rotational behavior after receptor stimulation by apomorphine, whereas contralateral rotations were observed after GP lesion. The alterations in dopamine and noradrenaline content of relating structures were determined by radiometric microassay. There was no strong correlation between transmitter depletion and motoric asymmetry. The site and extent of lesion seem to be more determinative in respect to motoric disturbances. 17 references. (Author abstract modified)

001713 Furgeson, Michael Douglas. University of Oklahoma Health Sciences Center **Importance of O-methylation in amphetamine-induced abnormal motor behavior in the rat.** (Ph.D. dissertation). Dissertation Abstracts International. 39(11):5633-B, 1979. Ann Arbor, Univ. Microfilms No. 7911808, 140p., 1978.

The role of the O-methylated metabolite of dopamine, 3-methoxytyramine, in the production of amphetamine-induced behavior was investigated in the context of amphetamine-induced abnormal behavior as a model for studies of drug-induced psychosis. Results of several experiments with rats indicate the necessity of some O-methylated compound in the production of dopamine-induced behavior and certain components of amphetamine-induced behavior. This role could indicate an importance for 3-methoxytyramine in the therapeutic action and side-effects of the major tranquilizers; in the symptomatology produced by chronic L-dopa therapy for Parkinson's disease; and in the induction of the schizophrenic episode. (Journal abstract modified)

001714 Galbicka, Gregory; Lee, Dennis M.; Branch, Marc N. Dept. of Psychology, University of Florida, Gainesville, FL **Schedule-dependent tolerance to behavioral effects of delta9-tetrahydrocannabinol when reinforcement frequencies are matched.** *Pharmacology Biochemistry and Behavior*. 12(1):85-91, 1980.

Schedule dependent tolerance to behavioral effects of delta9-tetrahydrocannabinol (delta9-THC) under a multiple schedule wherein reinforcement frequencies are matched are described. Squirrel monkeys pressed a lever under a multiple interresponse time greater than 28 seconds, modified random interval schedule which provided comparable frequencies and temporal distribution of food pellet presentation in the two components. Daily intramuscular administration of either 0.25 or 1.00mg/kg delta9-THC resulted initially in suppression and/or disruption of re-

sponding and concomitant decreases in the frequency of food presentation in both components. Responding in both components next increased, resulting in recovery of baseline frequencies of pellet delivery during the random interval component, but continued depression during the interresponse time schedule. The drug-induced changes in responding under the interresponse time schedule diminished with repeated injections, whereas response rates during the random interval schedule sometimes remained elevated. Interresponse time distributions under the interresponse time reinforcement frequency recovered to baseline levels. When drug injections were replaced by daily injections of the vehicle, responding was greatly disrupted only during the random interval component. These findings are only partially consistent with other results which suggest that tolerance development to the behavioral effects of delta9-THC is greatly enhanced if the drug initially produces reinforcement loss. 19 references. (Author abstract modified)

001715 Gale, Karen; Iadarola, Michael J. Georgetown University, School of Medicine, Dept. of Pharmacology, 3900 Reservoir Road, NW, Washington, DC 20007 **GABAergic denervation of rat substantia nigra: functional and pharmacological properties.** *Brain Research.* 183(1):217-223, 1980.

A modified hemisection technique was used to destroy fibers between the rat substantia nigra (SN) and striatum, without otherwise damaging nigral tissue. Data showed that the forebrain contribution to nigral GABA content was greater than 75%. Isoniazid-induced circling behavior, a functional response mediated by nigral GABA terminals, was abolished only when the GABA content of the SN was reduced by at least 80%. This was accomplished by blunt transection of all fibers connecting the SN with the ipsilateral forebrain. These lesions did not destroy GABA receptive nigral efferents mediating the behavioral circling response to intranigral muscimol. 24 references.

001716 Garey, R. E.; McQuitty, S.; Tootle, D.; Health, R. G. Tulane University School of Medicine, Dept. of Psychiatry and Neurology, 1430 Tulane Avenue, New Orleans, LA 70112 **The effects of apomorphine and haloperidol on PCP-induced behavioral and motor abnormalities in the rat.** *Life Sciences.* 26(4):277-284, 1980.

A series of experiments was conducted to compare the therapeutic efficacy of haloperidol and apomorphine on PCP-induced behavioral and motor abnormalities in the rat. Behavioral and motor dysfunctions induced by PCP were antagonized by both the DA agonist apomorphine and the DA antagonist haloperidol. In the test situation used, however, the antagonistic effects of apomorphine were much more rapid than those of haloperidol. Results suggest that PCP may be acting on specific presynaptic DA receptors and that this reaction is effectively antagonized by low doses of apomorphine in a manner similar to its effects in reducing schizophrenic symptoms and choreiform movement disorders. Results are discussed in relation to treatment of PCP-induced psychosis. 39 references. (Author abstract modified)

001717 Garzon, Javier; Fuentes, Jose A.; Del Rio, Joaquin. Dept. of Pharmacology, Institute of Medicinal Chemistry, CSIC, calle Juan de la Cierva no 3, Madrid-6, Spain **Antidepressants selectively antagonize the hyperactivity induced in rats by long-term isolation.** *European Journal of Pharmacology.* 59(3/4):293-296, 1979.

The effects of several classes of psychotropic drugs on the behavior induced in male Wistar rats by long-term isolation were examined. Rats isolated at 16 to 18 days of age showed after 10 to 12 months a complex behavioral syndrome marked by increased locomotor activity, compared to group housed controls. The hyperactivity of the socially deprived animals was blocked

by clinically effective antidepressants (amitriptyline, clomipramine, desipramine, doxepin, viloxazine, trazodone, phenelzine sulfate, and clorgyline), but not by antipsychotics (chlorpromazine and haloperidol), anxiolytics (chlordiazepoxide and diazepam), or amphetamine at doses that did not impair motor coordination. It is concluded that this animal model may be useful in detecting new antidepressant drugs, regardless of their mechanism of action, and in studying the etiology of depression. 10 references. (Author abstract modified)

001718 Gibson, Marie J.; Cheng, Mei-Fang. Institute of Animal Behavior, Rutgers University, 101 Warren Street, Newark, NJ 07102 **Neural mediation of estrogen-dependent courtship behavior in female ring doves.** *Journal of Comparative and Physiological Psychology.* 93(5):855-867, 1979.

The role played by the preoptic hypothalamic region in the mediation of female ring dove courtship behavior was investigated. Ovariectomized doves were tested in response to estradiol benzoate (EB) injections both before and after preoptic (POA) region, posterior medial hypothalamus (PMH), or sham lesions. Only the PMH group's behavior significantly declined following lesions. When EB implants were placed throughout the hypothalamic region, implants in the PMH were found to be most effective in stimulating behavior. The results indicate the importance of the PMH in mediation of estrogen dependent courtship behavior and are analogous to recent findings concerning the role of the ventromedial hypothalamus in mammalian female sexual behavior. 35 references. (Author abstract modified)

001719 Gleason, Phyllis E.; Michael, Sandra D.; Christian, John J. Department of Biological Sciences, State University of New York, Binghamton, NY 13901 **Effects of gonadal steroids on agonistic behavior of female *Peromyscus leucopus*.** *Hormones and Behavior.* 12(1):30-39, 1979.

The role of gonadal hormones in modifying agonistic behavior of female *Peromyscus leucopus* was examined by means of ovariectomy and treatment with estradiol benzoate (EB), progesterone (P), or testosterone propionate (TP). Aggression was lower in diestrous females than in proestrous females, and was eliminated by ovariectomy. Administration of EB had no effect on aggressive or submissive behavior, but higher dosages caused an increase in investigative and sexual behavior. Higher dosages of P increased aggression, as did higher dosages of TP. TP also caused an increase in investigative behavior, and had no effect on submissive behavior. It is suggested that these results may be due to direct effects of the administered hormones on behavior or to indirect effects such as a stimulation of prolactin secretion or alteration of adrenal function. 32 references. (Author abstract modified)

001720 Glick, Stanley D.; Cox, Russell D.; Maayani, Saul; Meibach, Richard C. Dept. of Pharmacology, Mount Sinai School of Medicine, CUNY, Fifth Avenue and 100th St., New York, NY 10029 **Anticholinergic behavioral effect of phencyclidine.** *European Journal of Pharmacology.* 59(1/2):103-106, 1979.

Phencyclidine (PCP) impaired spatial alternation performance in female Sprague-Dawley rats. This effect was mimicked by antimuscarinic anticholinergics (scopolamine and atropine) and by PCP derivatives (ketamine and cyclohexamine), but not by a variety of other agents. Muscarinic cholinergic agonists antagonized the effects of PCP. Results suggest that the effects of PCP on spatial alternation performance are mediated at least in part by an anticholinergic action. 13 references. (Author abstract modified)

001721 Goldberg, S. R.; Spealman, R. D.; Kelleher, R. T. NIDA, Addiction Research Center, P. O. Box 12390, Lexington-

ton, KY 40583 Enhancement of drug-seeking behavior by environmental stimuli associated with cocaine or morphine injections. *Neuropharmacology*. 18(12):1015-1017, 1979.

Brief visual stimuli that were occasionally contiguous with drug injections maintained high rates and characteristic fixed-ratio patterns of responding in squirrel monkeys under second-order schedules of cocaine or morphine injection. When the brief amber lights that were sometimes paired with drug injections were replaced by brief blue lights that were never paired with drug injections, the rates of responding declined and the fixed-ratio patterns of responding were disrupted. Rates of responding maintained by unpaired stimuli were higher than those seen in the absence of visual stimuli. Results indicate that pairing of brief stimuli with injections of cocaine or morphine can enhance the effectiveness of these stimuli in maintaining fixed-ratio responding and that drug seeking behavior can even be enhanced by unpaired stimuli that occur in regular association to sequences of responding leading to drug injection.

001722 Gordon, Frank J.; Brody, Michael J.; Fink, Gregory D.; Buggy, James; Johnson, Alan Kim. Dept. of Psychology, University of Iowa, Iowa City, IA 52242 Role of central catecholamines in the control of blood pressure and drinking behavior. *Brain Research*. 178(1):161-173, 1979.

The role of CNS catecholamines in the development of hypertension and the control of drinking behavior was assessed in male Sprague-Dawley rats. Intraventricular administration of 6-hydroxydopamine which depletes central catecholamines, completely prevented the development of one kidney renal hypertension and the associated increase in water consumptions. The treated rats also showed deficits in drinking behavior when challenged with subcutaneous injections of angiotensin-II (AII) and hypertonic sodium chloride. The acute pressor responses produced by intraventricular injections of AII and carbachol were abolished by central catecholamine depletion. Drinking produced by central cholinergic stimulation remained intact, but AII-induced drinking was significantly reduced. Results indicate that the integrity of CNS catecholamines is necessary for the development of one kidney renal hypertension and the increased drinking that accompanies it. 39 references. (Author abstract modified)

001723 Graeff, F. G.; Rawlins, J. N. P. Dept. of Pharmacology, School of Medicine, 14100-Ribeirao Preto, S. P., Brazil Dorsal periaqueductal gray punishment, septal lesions and the mode of action of minor tranquilizers. *Pharmacology Biochemistry and Behavior*. 12(1):41-45, 1980.

To study the role of the septo-hippocampal system and the dorsal periaqueductal gray (DPAG) substance in punished behavior and in the action of minor tranquilizers, two groups of rats were trained to lever-press on a continuous reinforcement schedule of food presentation. In one group, every response was subsequently punished by footshock delivery; in the other, by brief electrical stimulation of the DPAG of the mesencephalon. In both groups response rates were reduced to less than 10% of prepunishment rates, but not completely suppressed. Response rates did not significantly differ between the two groups, either before or after the introduction of punishment. Septal lesions significantly increased responding in the animals punished by foot shock but did not affect responding suppressed by DPAG stimulation. Injection of chlordiazepoxide (5mg/kg) significantly increased punished responding in both groups of rats, before as well as after the septal lesion. Before the septal lesion was made, responding suppressed by footshock was significantly more released by chlordiazepoxide than responding punished by DPAG stimulation. These results suggest that in punishment tests using footshock, both a behavioral inhibitory system, including the

septo-hippocampal structures and an aversive or punishment system, including the DPAG substance, act together to produce response suppression. Both these systems would be depressed by minor tranquilizers to cause their antipunishment and perhaps their antianxiety action as well. 32 references. (Author abstract)

001724 Graf, Laszlo; Miglec, Erzsebet; Bajusz, Sandor; Szekely, Jozsef I. Institute for Drug Research, H-1325 Budapest, P.O. Box 82, Hungary Met-enkephalin attenuates morphine tolerance in rats. *European Journal of Pharmacology*. 58(3):345-346, 1979.

The effects of met-enkephalin on tolerance to the analgesic effects of morphine were examined in male CFY rats. The analgesic response to morphine in the tail flick test was higher in rats chronically pretreated with equimolar amounts of morphine and met-enkephalin than in those pretreated with morphine alone. The attenuation of tolerance to morphine analgesia by met-enkephalin did not appear to be due to antagonism of receptor sites involved in morphine analgesia. It is speculated that specific interactions between enkephalin and beta-endorphin may account for the lack of tolerance and dependence on endogenous opioids with morphine-like pharmacological properties under physiological conditions. 5 references.

001725 Gray, Gary D.; Smith, Erla R.; Davidson, Julian M. Dept. of Physiology, Stanford University School of Medicine, Stanford, CA 94305 Hormonal regulation of penile erection in castrated male rats. *Physiology & Behavior*. 24(3):463-468, 1980.

The effects of various androgen agonists and antagonists on the restoration of penile erection in long-term castrated male rats were examined. Both testosterone and dihydrotestosterone (DHT) were very effective in restoring penile erections. Testosterone was also effective in restoring mating behavior, but DHT was totally ineffective. Estradiol was incapable of restoring erections but was effective in stimulating mounting behavior. The nonsteroidal antiandrogen flutamide inhibited the testosterone-induced restoration of penile erections; when administered alone, it had a slight excitatory effect. It is suggested that the androgen-induced restoration of penile erection derives more from neural changes than growth of somatic tissues, and the neural elements regulating erection demonstrate different response characteristics to various hormones than those regulating mounting. 24 references. (Author abstract modified)

001726 Green, Edward J.; Isaacson, Robert L.; Dunn, Adrian J.; Lanthorn, Thomas H. Isaacson: Dept. of Psychology, State University of New York, Binghamton, NY 13901 Naloxone and haloperidol reduce grooming occurring as an aftereffect of novelty. *Behavioral and Neural Biology*. 27(4):546-551, 1979.

The effects of naloxone and haloperidol on grooming behavior of the rat were investigated. Rats pretreated with naloxone or haloperidol exhibited less grooming than controls scored after handling and transported to a novel environment. Later, the same rats were pretreated with the same doses of naloxone or haloperidol and tested in an open-field hole board. Locomotion, exploration, and rearing scores of the drug treated animals were tested in their home cages in their familiar colony room after the moderate stress of handling, transport, and injection. The stress enhanced grooming was blocked by naloxone. It is concluded that mild to moderate stress may induce grooming without novelty per se, and that this effect is likely mediated by adrenocorticotrophic hormone acting in an agonist fashion on an opiate sensitive system. 8 references. (Author abstract modified)

001727 Greer, Charles August. University of Colorado at Boulder Dopaminergic modulation of the age-dependent effects of psychostimulants. (Ph.D. dissertation). Dissertation Abstracts International. 39(8):4088-B, 1979. Ann Arbor, Univ. Microfilms No. 7903049, 186p., 1978.

Dopaminergic modulation of age dependent effects of psychostimulants were investigated in five experiments in mice. In Experiment 1, the ontogeny of susceptibility to flurothyl-induced myoclonic and clonic seizures and amphetamine effects were examined in short and long sleep mice. In Experiment 2, neuropharmacological analyses were conducted in 30 and 120-day-old mice to elucidate the substrates of age dependent response to amphetamine in short sleep mice. Experiment 3 examined the generalizability of these amphetamine effects to other psychostimulants (cocaine, nicotine, and strychnine). Experiment 4 established the role of DA in these age dependent responses by examining the effects of haloperidol on cocaine, amphetamine, strychnine, and nicotine. Finally, Experiment 5 examined age dependent effects of amphetamine on open-field activity of short sleep mice. Collectively these experiments demonstrated that dopaminergic systems in short sleep mice undergo substantial alterations over the course of development. (Journal abstract modified)

001728 Harris, R. Adron; Snell, Diane. University of Missouri School of Medicine, Columbia, MO 65212 Effects of acute and chronic administration of phenobarbital and d-amphetamine on schedule-controlled behavior. *Pharmacology Biochemistry and Behavior*. 12(1):47-52, 1980.

The effects of acute and chronic administration of phenobarbital and d-amphetamine were determined in rats responding under a multiple interval 5 minute fixed-ratio 30 (Mult FI5/FR30) schedule of food presentation. After determining the acute effects of each drug, the drugs were injected daily with one group of rats receiving the drugs before each behavioral session while another group received the drugs immediately after each daily session. After four to seven consecutive injections, tolerance developed to the effects of phenobarbital on the average rates of responding under RI and FR schedule components only if the drug was administered before each session. Tolerance was more pronounced for responding during the terminal portions of the FI component than for responding during either the initial portions of the FI or the FR component. Evidence for a selective tolerance to the effects of the drug on responding during the final segments of the FI was also obtained in rats responding under an FI5 schedule. In contrast, injection of d-amphetamine for 7 to 8 consecutive days failed to produce any tolerance to the effects of the drug on responding under FI5/FR30, FI5 or FR30 schedules. These results indicate that the development of tolerance to the effects of phenobarbital depends both upon the temporal relationship of the drug effects to the behavioral testing and upon the schedules controlling behavior. These findings are discussed in terms of theories of behavioral tolerance. 14 references. (Author abstract)

001729 Heal, D. J.; Green, A. R.; Buylaert, W. A. University Dept. of Clinical Pharmacology, Radcliffe Infirmary, Oxford OX2 6HE, England Inhibition of apomorphine-, bromocriptine- and lergotril-induced circling behaviour in rats by subsequent haloperidol administration. *Neuropharmacology*. 19(1):133-137, 1980.

In male Sprague-Dawley rats with unilateral nigrostriatal lesions, circling behavior induced by apomorphine (0.5mg/kg) was markedly inhibited by treatment with haloperidol (0.5 or 1.0mg/kg) either 10 minutes before or 10 minutes after the apomorphine. Haloperidol pretreatment also inhibited circling induced in these animals by bromocriptine or lergotril. Circling behavior induced by the ergot drugs was also inhibited by haloperidol given 90 minutes after the onset of turning. 5 references. (Author abstract modified)

001730 Heller, Knud Erik. Zoological Laboratory, University of Copenhagen, Universitetsparken 15, DK-2100 Copenhagen,

Denmark An attempt to separate the roles of corticosterone and ACTH in the control of post-shock fighting behaviour in male laboratory mice. *Behavioural Processes*. 4(3):231-238, 1979.

One experiment was conducted to separate the roles of corticosterone and ACTH in the mediation of the facilitatory effects of experiencing shock on subsequent fighting behavior in male mice. It was found that treatment with electric foot shock and single injections of ACTH led to comparable increases in subsequent fighting in intact males; preventing changes in testosterone secretion by combined castration and testosterone replacement does not occlude or modify the facilitatory effects of shock or ACTH on subsequent fighting; and preventing changes in both testosterone and corticosterone secretion by combined castration/adrenalectomy and testosterone/corticosterone replacement prevents shock and ACTH-induced increases in fighting. These findings suggest that corticosterone plays a more important role than ACTH in the mediation of the facilitatory effects of shock on subsequent fighting behavior in male mice. 22 references. (Author abstract)

001731 Hemmingsen, Ralf; Sorensen, Soren C. Dept. of Psychiatry, Psychochemistry Institute, Rigshospitalet, DK-2100 Copenhagen, Denmark Absence of an effect of naloxone on ethanol intoxication and withdrawal reactions. *Acta Pharmacologica et Toxicologica*. 46(1):62-65, 1980.

The effects of naloxone on signs of severe ethanol intoxication and on the withdrawal syndrome following chronic ethanol intoxication were examined in male Wistar rats. No differences in level of intoxication or severity of withdrawal symptoms were found between saline treated rats and those given 2mg/kg i.p. naloxone every 6 hours. These findings do not rule out a biochemical link between the actions of ethanol and opiates, but do suggest that this link is not localized at the level of specific drug receptor interaction. 16 references. (Author abstract modified)

001732 Hershkowitz, Moshe; Szechtman, Henry. Dept. of Pharmacology, School of Medicine, Tel-Aviv University, Tel-Aviv, Israel Pretreatment with delta1-tetrahydrocannabinol and psychoactive drugs: effects of uptake of biogenic amines and on behavior. *European Journal of Pharmacology*. 59(3/4):267-276, 1979.

The injection of delta1-tetrahydrocannabinol (THC) into male Balb/c mice increased the uptake into brain synaptosomes of radioactive dopamine (DA), norepinephrine, serotonin, and GABA, but not of leucine. The effect of marijuana compounds on DA uptake was correlated with their psychoactive potency. THC caused a greater increase in DA uptake in cortical synaptosomes than in striatal synaptosomes. THC caused a dose dependent inhibition of stereotyped behaviors induced by tail pinch in male Wistar rats, but did not antagonize stereotypy induced by apomorphine or amphetamine in mice. However, amphetamine and apomorphine did appear to reverse the sedation induced by THC. Results suggest that THC acts by blocking receptors in several cortical neurotransmitter systems, rather than by blocking monoamine oxidase uptake, releasing transmitters, or directly stimulating uptake. 28 references. (Author abstract modified)

001733 Ho, W. K. K.; Wong, H. K.; Wen, H. L. Dept. of Biochemistry, Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China The influence of electroacupuncture on naloxone-induced morphine withdrawal - III. The effect of cyclic AMP. *Neuropharmacology*. 18(11):865-869, 1979.

The role of cyclic AMP in the treatment of morphine addiction by electroacupuncture was studied in female WHT mice and Sprague-Dawley rats. A significant drop of plasma cyclic AMP during addiction and a dramatic rise in plasma cyclic

AMP during withdrawal were observed. Electroacupuncture suppressed withdrawal behavior, but this effect was completely antagonized by subcutaneous pretreatment with a phosphodiesterase inhibitor or intracerebral injection of dibutyl cyclic AMP. The involvement of cyclic AMP and endorphins in electroacupuncture and morphine withdrawal is discussed. 17 references. (Author abstract modified)

001734 Holzer, Peter; Jurna, Ilmar; Gamse, Rainer; Lembeck, Fred. Institut für Experimentelle und Klinische Pharmakologie der Universität Graz, Universitätsplatz 4, A-8010 Graz, Austria. **Noiceptive threshold after neonatal capsaicin treatment.** *European Journal of Pharmacology*. 58(4):511-514, 1979.

The nociceptive threshold was determined by measuring reaction time in the hot plate and tail flick tests 3 to 4 months after treatment of young Sprague-Dawley rats with capsaicin (50mg/kg, subcutaneously). Reaction time in the tail flick test was prolonged in rats pretreated with capsaicin on the second day of life. Capsaicin pretreatment up to the tenth day of life also prolonged reaction time in the hot plate test, but capsaicin treatment after day 10 had no effect. The elevation of the nociceptive threshold after neonatal capsaicin treatment may reflect degeneration of the afferent nerve fibers activated by noxious stimuli. 10 references. (Author abstract modified)

001735 Horton, Roger W.; Collins, James F.; Anlezark, Gillian M.; Meldrum, Brian S. Dept. of Neurology, Institute of Psychiatry, London SE5 8AF, England. **Convulsant and anticonvulsant actions in DBA/2 mice of compounds blocking the reuptake of GABA.** *European Journal of Pharmacology*. 59(1/2):75-83, 1979.

The convulsant and anticonvulsant activities of compounds that block the uptake of GABA into neurons or glia were determined in 21 to 28-day-old DBA/2 mice, which are genetically susceptible to audiogenic seizures. Protection against sound-induced seizures was seen after intracerebroventricular (i.c.v.) injection of (+)-2,4-diaminobutyric acid, (+ or -)nipecotic acid, (+)-ethyl nipecotate, (-)-piperazine acid, putrescine and after i.p. injection of (+)-2,4-diaminobutyric acid and (+)-ethyl nipecotate. Nipecotate and nipecotic acid were the most effective anticonvulsants when given i.c.v., but nipecotic acid was ineffective when given i.p. Limb myoclonus and other epileptic manifestations (rearing, wild running, and tonic clonic seizures) occurred in the absence of auditory stimulation after (+)-2,4-diaminobutyric acid, (+ or -)-cis-3-aminocyclohexane carboxylic acid, and putrescine. Beta-alanine depressed respiration but did not protect against audiogenic seizures or induce myoclonus. 30 references. (Author abstract modified)

001736 Hutchison, Victor H.; Black, Jerry J.; Erskine, Dale. Department of Zoology, University of Oklahoma, Norman, OK 73019. **Melatonin and chlorpromazine: thermal selection in the mudpuppy, *necturus maculosus*.** *Life Sciences*. 25(6):527-530, 1979.

The influence of exogenous and endogenous melatonin on the diel cycles of temperature selection of the mudpuppy was studied. Intraperitoneal injections of melatonin and chlorpromazine, which blocks the breakdown of endogenous melatonin, significantly decreased temperatures selected by salamanders in a linear thermal gradient and eliminated the normal diel cycle in behavioral thermoregulation shown by control animals. It is suggested that both endogenous and exogenous melatonin may play a crucial role in both physiological and behavioral thermoregulation of vertebrates. 22 references. (Author abstract modified)

001737 Isaac, Walter; Kallman, Mary D. Department of Pharmacology, Medical College of Virginia, Richmond, VA. **Locomotor effects of d-amphetamine and methylphenidate in young**

squirrel monkeys. *Bulletin of the Psychonomic Society*. 14(4):315-317, 1979.

The effects of d-amphetamine and methylphenidate upon the locomotor activity of six young squirrel monkeys were studied. While d-amphetamine produced a dose related decrease in activity, methylphenidate produced no significant changes. Combined doses of the drugs, as well as a large dose of methylphenidate, produced no changes in locomotor activity related to methylphenidate. 14 references. (Author abstract)

001738 Izquierdo, Ivan; Graudenz, Marcia. Departamento de Bioquímica, Instituto de Biociências, U. F. R. G. S. (centro), 90000 Porto Alegre, RS, Brazil. **Memory facilitation by naloxone is due to release of dopaminergic and beta-adrenergic systems from tonic inhibition.** *Psychopharmacology*. 67(3):265-268, 1980.

The influence of release of dopaminergic and beta-adrenergic systems from tonic inhibition on memory facilitation by naloxone was investigated. The posttraining IP administration of naloxone was found to facilitate memory consolidation of the habituation of a rearing response to a tone in rats. Amphetamine or nicotine and amphetamine plus nicotine have no effect. The higher doses of amphetamine or nicotine, however, when given together with a dose of naloxone which is ineffective alone, markedly enhanced consolidation. Haloperidol, propranolol, and phenoxybenzamine had no effect of their own; whereas tolazoline impaired consolidation. The effect of naloxone was antagonized by haloperidol and by propranolol, but not by phenoxybenzamine or tolazoline. Results suggest that naloxone causes memory facilitation through the release of central dopaminergic and beta adrenergic mechanisms from a tonic inhibitory influence of endogenous opiate peptide systems. 23 references. (Author abstract modified)

001739 Izquierdo, Ivan; Paiva, Antonio C. M.; Elisabetsky, Elaine. Departamento de Bioquímica, Instituto de Biociências, UFRGS (centro), 90000 Porto Alegre, RS, Brazil. **Post-training intraperitoneal administration of Leu-enkephalin and beta-endorphin causes retrograde amnesia for two different tasks in rats.** *Behavioral and Neural Biology*. 28(2):246-250, 1980.

The immediate posttraining administration of Leu-enkephalin or of beta-endorphin (10mcg/kg, ip) in rats was found to cause retrograde amnesia, both for the habituation of rearing response to a tone, and for shuttle avoidance behavior. The facts that the doses employed were very low, and that in previous papers the opiate antagonist, naloxone, was found to have an opposite effect, suggest that endogenous opiates are physiologically active amnesic agents. 5 references. (Author abstract)

001740 Jarbe, T. U. C.; McMillan, D. E. Dept. of Psychology, University of Uppsala, P. O. Box 227, S-751 04, Uppsala, Sweden. **Discriminative stimulus properties of tetrahydrocannabinols and related drugs in rats and pigeons.** *Neuropharmacology*. 18(12):1023-1024, 1979.

The discriminative stimulus properties of delta9-tetrahydrocannabinol (delta9-THC), the soluble THC derivative SP-111, and the THC metabolites 11-hydroxy-delta9-THC, 11-hydroxy-delta8-THC, 8alpha-hydroxy-delta9-THC, 8beta-hydroxy-delta9-THC, 8alpha,11-dihydroxy-delta9-THC, and 8beta,11-dihydroxy-delta9-THC were compared. Substitution tests with the 11-hydroxylated metabolites in rats and pigeons produced dose related generalization gradients, with 11-hydroxy-delta9-THC, 11-hydroxy-delta8-THC, and delta9-THC in decreasing order of potency. Among the other metabolites, only 8beta,11-dihydroxy-delta9-THC resulted in generalization to the delta9-THC stimulus. The effects of SP-111 varied with the time of action and showed that SP-111 had a slower onset of action than delta9-THC. 8 references.

001741 Jefferys, D.; Oei, T. P. S.; Singer, G. Singer. Dept. of Psychology, La Trobe University, Bundoora, Victoria, 3083, Australia **A reconsideration of the concept of drug dependence.** *Neuroscience and Biobehavioral Reviews*. 3(3):149-153, 1979.

The schedule-induced self-injection (SiSi) model for investigating drug dependency is discussed. In this experimental paradigm, self-injection of drugs is examined in animals with reduced body weight and catheterized jugular vein, on a fixed time food delivery schedule. This model permits isolation of critical patterns of interaction between pharmacological and environmental factors involved in drug seeking behavior. The SiSi model of dependence may be relevant to the analysis of human drug abuse, providing a means of predicting the abuse potential of new psychoactive drugs, assessing pharmacological and environmental factors that might diminish drug seeking behavior, and investigating the biological and behavioral mechanisms underlying drug abuse. 39 references. (Author abstract modified)

001742 Johnson, F. N. Dept. of Psychology, University of Lancaster, Bailrigg, Lancaster LA1 4YF, England **The effects of lithium chloride on spontaneous alternation behaviour in the goldfish (*Carassius auratus*).** *Neuropsychobiology*. 6(2):72-78, 1980.

The question of whether lithium has an adverse effect upon the establishment of memory traces was examined. Spontaneous alternation behavior of goldfish was observed in a two unit T maze. While significant degrees of alternation occurred under both lithium and sodium treatment, alternation under lithium was significantly lower than under sodium. In a second experiment it was shown that lithium increased the amount of random or erratic behavior demonstrated by fish. The effects of lithium on spontaneous alternation were fully explained by a lithium-induced increase in randomness of activity, without recourse to any assumption that lithium affected memory traces. 19 references. (Author abstract modified)

001743 Jolles, J.; Rompa-Barendregt, J.; Gispen, W. H. Rudolf Magnus Institute for Pharmacology, State University of Utrecht, Padualaan 8, Utrecht, The Netherlands **ACTH-induced excessive grooming in the rat: the influence of environmental and motivational factors.** *Hormones and Behavior*. 12(1):60-72, 1979.

The role of environmental and motivational factors in adrenocorticotrophic hormone (ACTH) induced excessive grooming was examined. Intraventricularly administered ACTH1-24 in rats initiated excessive grooming followed by stretching and yawning syndrome. Novelty was not an essential prerequisite for its expression, and a variety of environmental variables was not able to influence the peptide-induced behavior. Only very strong motivational variables as severe hunger/thirst and anxiety were able to modulate the grooming. This response was significantly depressed in water deprived rats bar-pressing for water in a Skinner box, as well as in rats receiving unavoidable electric foot shock. Results suggest that excessive grooming is a secondary response serving to dearouse the organism after activation by ACTH and is indicative of the strength of ACTH-induced motivation to groom. 33 references. (Author abstract modified)

001744 Jones, Douglas L.; Mogenson, Gordon J. Dept. of Physiology, University of Western Ontario, London, Ontario, Canada N6A 5C1 **Oral motor performance following central dopamine receptor blockade.** *European Journal of Pharmacology*. 59(1/2):11-21, 1979.

Oral motor responses were recorded in water deprived male Wistar rats following injection of the dopamine receptor blocker spiroperidol into the nucleus accumbens and caudate nucleus. When injected into the nucleus accumbens, spiroperidol produced a dose dependent decrease in lap volume and tongue ex-

tension. Injections into adjacent sites or into the caudate nucleus failed to significantly reduce lap volume, even when high doses were used. Results implicate the mesolimbic dopaminergic projections to the nucleus accumbens in oral motor responses and indicate the need for systemic comparisons of the contributions of mesolimbic and nigrostriatal dopaminergic systems to ingestive behaviors. 36 references. (Author abstract modified)

001745 Kaplan, Ronald Jay. Illinois Institute of Technology **The effects of testosterone, dihydrotestosterone, estrogen, and nitromifene citrate on aggressive behavior in male hamsters. (Ph.D. dissertation).** *Dissertation Abstracts International*. 39(8):4090-B, 1979. Ann Arbor, Univ. Microfilms No. 7902998, 89p., 1978.

The effects of testosterone propionate (TP), estradiol benzoate (EB), and dihydrotestosterone (DHT) on aggressive behavior were examined in gonadectomized male hamsters. TP, EB, and DHT, when combined with placebo, were all found effective in reinstating various aspects of intraspecific aggression in group caged hamsters. Lower doses proved as effective as higher doses. The antiestrogen, nitromifene citrate, proved an effective competitive inhibitor in suppressing TP, EB, and DHT-induced aggressive behavior. The degree of suppression of steroids was found to be a function of dose or hormone, with lower doses showing greater suppression. DHT proved to have central effects, and estrogen appeared to influence aggression independently of androgen. Daily injections of hormone with placebo resulted in weight gain in some males. Males treated with lower doses of EB and DHT weighed more at the end of the experiments than did hamsters treated with other steroids. (Journal abstract modified)

001746 Kareti, Sarala; Moreton, J. E.; Khazan, N. Dept. of Pharmacology and Toxicology, University of Maryland School of Pharmacy, Baltimore, MD 21201 **Effects of buprenorphine, a new narcotic agonist-antagonist analgesic on the EEG, power spectrum and behavior of the rat.** *Neuropharmacology*. 19(2):195-201, 1980.

The acute effects of buprenorphine, a new narcotic agonist/antagonist, on the CNS were investigated in unanesthetized, freely moving rats, utilizing EEG and behavioral parameters. Rats were prepared with chronic cortical and temporalis muscle electrodes for continuous recording of EEG, EMG, and gross behavior for 3 days before and 3 to 4 days after acute intravenous administration of physiological saline, morphine, or buprenorphine at several doses. Generally, narcotic agonists, like morphine, produce a biphasic pattern of initial behavioral stupor with high voltage EEG slow bursting activity, followed by behavioral arousal with low voltage desynchronous EEG. In the present study, buprenorphine, a partial agonist of the morphine type, produced a similar biphasic effect at low doses; but on quantitation of duration of stupor and arousal, an inverted U shaped function resulted. Increasing doses up to 1mg/kg increased the duration of stupor to a maximum, and further increase to 10 or 30mg/kg decreased the duration of stupor. Also, increasing doses up to 10mg/kg increased the duration of arousal to a maximum, but increase to 30mg/kg actually decreased the duration of arousal. Computer derived EEG spectral power between 0 and 10Hz also showed an inverted U shaped relation to doses from 0.3 to 10mg/kg, with a maximal power at 1mg/kg associated with maximal EEG synchrony. These findings demonstrate a dose dependent agonist/antagonist action of buprenorphine. At low to intermediate doses, it has narcotic agonist action, but at higher doses, it manifests antagonistic action by blocking its own agonist effects. 16 references. (Author abstract modified)

001747 Katz, Jonathan L. Laboratory of Psychobiology, Dept. of Psychiatry, Harvard Medical School, 25 Shattuck St.,

Boston, MA 02115 A comparison of responding maintained under second-order schedules of intramuscular cocaine injection or food presentation in squirrel monkeys. *Journal of the Experimental Analysis of Behavior*. 32(3):419-431, 1979.

Keypressing by squirrel monkeys was maintained under second order schedules of either intramuscular cocaine injection or food presentation. There was little difference between cocaine and food maintained responding in the effects of brief stimulus changes on responding within a particular schedule condition. Across schedules and regardless of maintaining events, there were marked differences in the way changes in brief stimuli changed performances. With the influence of cocaine injections and subsequent responding precluded, it is concluded that performances maintained under second-order schedules with cocaine or food are not only similar, but also depend similarly on the particular schedule under which they are presented. 28 references. (Author abstract modified)

001748 Katz, R. J. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 Hypophysectomy reduces behavioral activation to morphine in the rat. *Behavioral and Neural Biology*. 28(3):361-365, 1980.

In an examination of the behavioral effects of morphine in the rat, chronically maintained hypophysectomized or sham operated adult male Sprague-Dawley rats were injected with vehicle or one of two doses of morphine. Motor activity was remotely recorded for 100 minutes after injection. Activity was markedly reduced by prior pituitary removal. It is concluded that this finding is consistent with previous studies utilizing other models of pituitary opiate interactions. 9 references. (Author abstract)

001749 Katz, R. J.; Roth, K. A.; Schmaltz, K.; Sible, M. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 Interaction of stress and morphine in the rat using a classical conditioning design. *Behavioral and Neural Biology*. 28(3):366-371, 1980.

The effect of stressful but not immediately painful stimulation upon an opiate mediated syndrome was examined in the rat with the use of a novel procedure. Noise stress and morphine administration were factorially varied in the classical conditioning of environmental preference in a two choice apparatus. In comparison with control subjects which showed no change, morphine produced a preference shift toward the conditioned environment which was further potentiated by a noise stimulation. It is concluded that stress may potentiate the reinforcing effects of opiate alkaloids. 20 references. (Author abstract modified)

001750 Katz, Richard. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 Grooming elicited by intracerebroventricular bombesin and eledoisin in the mouse. *Neuropharmacology*. 19(1):143-146, 1980.

The behavioral effects of centrally administered bombesin and eledoisin, two peptides derived from amphibian skin, were investigated in male Swiss-Webster mice. Both peptides produced compulsive stereotyped grooming syndromes, which were not modified by morphine or naloxone. These findings demonstrate the existence of a novel, nonopioid form of neuropeptide mediated grooming behavior. 12 references. (Author abstract modified)

001751 Kelley, Ann E.; Iversen, Susan D. Mailman Research Laboratories, McLean Hospital, Belmont, MA Substance P infusion into substantia nigra of the rat: behavioural analysis and involvement of striatal dopamine. *European Journal of Pharmacology* 60(2/3):171-179, 1979.

The open-field behavior of male Sprague-Dawley rats with 6-hydroxydopamine lesions of the caudate nucleus and rats with sham lesions was evaluated following bilateral infusion of substance-P (SP) into the substantia nigra. In the sham lesioned rats, the first infusion produced a strong increase in stereotyped rearing and sniffing, with no concurrent enhancement of locomotion. With three subsequent infusions at 2 day intervals, the rearing response disappeared and a tendency to groom emerged. All SP-induced behavioral stimulation was blocked in the caudate lesioned rats, and the lesion itself reduced rearing. Results suggest that the response to SP infusion was mediated through the nigrostriatal dopamine system. 32 references. (Author abstract modified)

001752 Kelley, Ann E.; Stinus, Louis; Iversen, Susan D. Mailman Research Laboratories, McLean Hospital, Belmont, MA Interaction between D-Ala-Met-enkephalin, A10 dopaminergic neurones, and spontaneous behaviour in the rat. *Behavioural Brain Research*. 1(1):3-24, 1980.

The interaction between opioid peptides and dopaminergic A10 (DA-A10) neurons in the ventral tegmental area (VTA) was investigated, and the behavioral consequences of VTA infusion of D-Ala-Met-enkephalinamide (DALA) were analyzed. DALA elicited a dose dependent increase in locomotor activity measured in photocell cages and the circular corridor. Observations in the open field and in a hole box revealed that DALA-induced behavioral stimulations were characterized by enhancement of locomotion, rearing, and number of hole visits, while grooming time and duration of hole visits were decreased. DALA-induced stimulation was reserved by naloxone, and was completely blocked by 6-OHDA destruction of DA-A10 terminals. D-amphetamine-induced behavioral activation was potentiated by simultaneous VTA infusions of DALA which indicates that the behavioral response to DALA is dependent on DA-A10 neuronal activity. It is postulated that stimulation of opiate receptors exerts a presynaptic inhibition of an inhibitory input to DA-A10 neurons (e.g. GABA or dendritic DA), thus releasing dopaminergic activity. In contrast to the acute effect, the D-amphetamine response was strongly attenuated 4 hours and 1 and 6 days after VTA infusion of DALA, and returned to normal only at 14 days. This long lasting modification may reflect decreased activity of opioid neurons, releasing the inhibition of DA-A10 neurons. Findings suggest that endogenous opioid peptides may exert a modulatory influence on the dopaminergic mesocorticolimbic system. 75 references. (Author abstract modified)

001753 Kiefer, Stephen W.; Braun, J. Jay. Braun: Dept. of Psychology, Arizona State University, Tempe, AZ 85281 Acquisition of taste avoidance habits in rats lacking gustatory neocortex. *Physiological Psychology*. 7(3):245-250, 1979.

Normal rats and rats lacking gustatory neocortex were compared in the discriminative acquisition of aversions to either a .146 M sucrose solution or a .153 M sodium chloride solution. Training involved repeated pairings of one taste solution with injections of apomorphine hydrochloride during restricted periods of fluid access. Rats lacking gustatory neocortex acquired discriminatively specific aversions to sucrose and sodium chloride, but compared to normal control subjects, they acquired the aversions more slowly and they generalized more to the unpaired taste solution. The results confirm earlier suggestions that gustatory neocortex lesions disrupt the associative salience of specific taste stimuli. In addition, these results also clarify the nature of the deficit by showing that it appears to be relative rather than absolute. 25 references. (Author abstract modified)

001754 Kiianmaa, K.; Attila, L. M. J. Research Laboratories of the State Alcohol Monopoly, Box 350, SF-00101 Helsinki 10,

Finland Alcohol intake, ethanol-induced narcosis and intoxication in rats following neonatal 6-hydroxydopamine or 5,7-dihydroxytryptamine treatment. Naunyn-Schmiedeberg's Archives of Pharmacology. 308(2):165-170, 1979.

Newborn rats were treated with 5,7-dihydroxytryptamine (5,7-HT) after pretreatment with desipramine for depletion of brain 5-HT or with 6-hydroxydopamine (6-OHDA) for selective reduction of brain noradrenaline (NA). The 5,7-HT resulted in a 54% reduction in endogenous 5-HT in the cerebral cortex and a 60% increase in pons medulla when determined in adult rats. The 5-HT content in the midbrain was not affected. Endogenous NA in 6-OHDA treated animals was selectively reduced by 100% in the cerebral cortex, 35% in the midbrain, and increased 117% in the pons medulla. No difference was found in voluntary ethanol selection of these groups and controls at 3 months old. In a tilting plane test, ethanol impaired performance of the 6-OHDA rats significantly more than controls and also produced significantly longer narcosis. In contrast, 5,7-HT rats were not affected significantly more than controls in these tests. Results suggest that catecholamine neuronal systems interact with the expression of alcohol intoxication. 32 references. (Author abstract modified)

001755 Koenigshofer, Kenneth Andrew. University of California, Riverside **Dopaminergic and cholinergic factors controlling amphetamine aversiveness in the conditioned taste aversion experiment: an animal model for the detection of neuroleptic potency and extrapyramidal disturbance?** (Ph.D. dissertation). Dissertation Abstracts International. 40(2):970-B, 1979. Ann Arbor, Univ. Microfilms No. 7918250, 87p., 1979.

Neuropharmacological bases for the punishing effects of amphetamine in the conditioned taste aversion (CTA) paradigm were investigated, and the roles of specific neurotransmitters were reexamined. In Experiment 1, the relative roles of noradrenergic (NE) and dopaminergic (DA) systems in the mediation of amphetamine aversiveness in the CTA paradigm were examined. Results indicate that DA systems mediate both aversive and reinforcing properties of amphetamine. In Experiment 2, the role of DA mechanisms was confirmed by the demonstration that the DA receptor blocker, pimozone, not only attenuated acquisition of aversion evoked by amphetamine, but also that evoked by the known DA agonist, apomorphine. In Experiment 3, the use of amphetamine in the CTA was evaluated as an animal model for detection of drugs with antipsychotic potency in humans. (Journal abstract modified)

001756 Kokkinidis, Larry Platon. Carleton University (Canada) **Effects of acute and chronic amphetamine administration: behavioral and neurochemical specificity.** (Ph.D. dissertation). Dissertation Abstracts International. 39(11):5615-B, 1979. (Not available from Univ. Microfilms), 1978.

The behavioral and neurochemical specificity of acute and chronic amphetamine administration was assessed in rats via open-field and Y-maze behavioral measures. Data are presented which indicate that startle reflex, rotational behavior, perseveration, and shock-induced reactivity involve primarily noradrenergic activity, whereas stereotypy and sensitization effects in a reactivity task are dependent upon dopaminergic mechanisms. It is hypothesized that tolerance occurs principally to behaviors which involve noradrenergic activity. (Journal abstract modified)

001757 Koller, W. C.; Weiner, W. J.; Klawans, H. L.; Nausieda, P. A. Dept. of Neurological Sciences and Pharmacology, Rush-Presbyterian St. Luke's Medical Center, 1725 West Harrison Street, Chicago, IL 60612 **Influence of female sex hormones**

on neuroleptic-induced behavioral supersensitivity. Neuropharmacology. 19(4):387-391, 1980.

The influence of various states of female sex hormones on the development of neuroleptic-induced behavioral supersensitivity to a dopamine agonist was investigated. The chronic administration of haloperidol-induced behavioral hypersensitivity in male guinea-pigs. This effect has often been reported with male animals. In female guinea-pigs, haloperidol failed to induce any behavioral changes. Oophorectomy of female guinea-pigs significantly reduced the behavioral response to apomorphine when compared to normal female animals. This behavioral hyposensitivity increased as a function of time after oophorectomy. Chronic haloperidol treatment in oophorectomized animals produced behavioral hypersensitivity. Chronic treatment of either estradiol or progesterone in oophorectomized animals caused a significant enhancement of the behavioral response. In oophorectomized animals treated chronically with estradiol plus haloperidol or progesterone plus haloperidol, no greater behavioral response was observed than with treatment with estradiol or progesterone alone. These results suggest that female sex hormones are able to modify dopamine receptor sensitivity and alter the development of behavioral supersensitivity induced by neuroleptics. 26 references. (Author abstract)

001758 Kornetsky, Conan; Esposito, Ralph U. Boston University School of Medicine, Boston, MA 02118 **Euphorogenic drugs: effects on the reward pathways of the brain.** Federation Proceedings. 38(11):2473-2476, 1979.

Studies of the effects of morphine, narcotic agonists/antagonists, cocaine, d-amphetamine, and phencyclidine on the threshold for intracranial self-stimulation (ICSS) in rats are summarized. Morphine lowered the threshold for ICSS, with little or no tolerance to this effect. The only mixed agonist/antagonist that lowered the ICSS threshold was pentazocine. The ICSS threshold was also lowered by cocaine and d-amphetamine and, to a lesser extent, phencyclidine. Results suggest that the abuse liability of these agents may be directly related to their ability to sensitize the neural substrate involved in natural reward. 21 references. (Author abstract modified)

001759 Kovacs, G. L.; Vecsei, L.; Medve, L.; Telegdy, G. Telegdy, Dept. of Pathophysiology, University Medical School, P.O.B. 531, H-6701 Szeged, Hungary **Effect on memory processes of anti-vasopressin serum microinjected into the dorsal raphe nucleus: the role of catecholaminergic neurotransmission.** Experimental Brain Research. 38(3):357-361, 1980.

The effect on memory processes of antivasopressin serum microinjected into the dorsal raphe nucleus of male CFY rats was investigated. Anti-arginine8-vasopressin serum was microinjected into the mesencephalic dorsal raphe nucleus immediately after the learning trial, in a one trial learning passive avoidance reaction. The treatment attenuated passive avoidance behavior 24 hours after treatment, suggesting a role of the endogenous vasopressin of this area in memory processes. On the other hand, the antiserum did not influence passive avoidance behavior if 6-hydroxydopamine was microinjected into the raphe region. Data suggest that the antiserum may have primarily interacted with catecholaminergic terminals, which enter the dorsal raphe nucleus. 31 references. (Author abstract modified)

001760 Koven, Sheldon Jack. University of Manitoba (Canada) **The involvement of cholinergic mechanisms in morphine dependency.** (Ph.D. dissertation). Dissertation Abstracts International. 40(8):3688-B, 1980. (Not available from Univ. Microfilms), 1979.

The involvement of cholinergic mechanisms in morphine dependency was examined. Antagonist precipitated jumping in mice, as well as in rats, was significantly reduced in choline pre-

treated animals. The optimal dose of this partial agonist differed as a function of the rate and extent of development of morphine dependency. Using similar testing procedures, an anomalous, antinociceptive effect of naloxone was observed at very low doses. This result represents one of the earliest demonstrations of an interaction between an exogenous opiate antagonist and a deliberate experimental provocation of endogenous opioid release. (Journal abstract modified)

001761 Krehbiel, Dwight A.; LeRoy, L. Michael. Department of Psychology, Bethel College, North Newton, KS 67117 **The quality of hormonally stimulated maternal behavior in ovariectomized rats.** *Hormones and Behavior*. 12(3):243-252, 1979.

Maternal behavior was induced in ovariectomized female rats through injections of estradiol, progesterone, and prolactin followed by continuous pup exposure. This behavior was compared with that of pup exposed, vehicle injected ovariectomized females and of parturient females on a wide variety of measures. The hormone injections did not significantly reduce retrieval latency. However, the performance of hormone injected females on other measures, especially measures of pup directed behaviors and of nest building, was markedly superior to that of ovariectomized females and similar to that of parturient animals. These results suggest that the hormonal factors which normally facilitate rapid onset of maternal behavior may not be identical to those affecting the quality of the behavior displayed. 20 references. (Author abstract)

001762 Kripke, Daniel, F.; Wyborney, V. Grant. Veterans Administration Medical Center (V116), San Diego, CA 92093 **Lithium slows rat circadian activity rhythms.** *Life Sciences*. 26(16):1319-1321, 1980.

The effects of lithium carbonate on the free running circadian wheel running rhythm of blinded laboratory rats were investigated. Twenty-eight male Sprague-Dawley rats were blinded by enucleation under sodium methohexital anesthesia and placed in separate sound isolated recording cages. Half were fed lithium biscuits formed by adding 600mg lithium carbonate to 200g pulverized Purina Rat Chow. Each animal was left undisturbed in a continuously lighted recording cage for approximately 3 weeks while running wheel revolutions were monitored continuously. For each 24 hours of data, the best fitting 24 hour cosine was estimated by a least squared technique, and the average acrophase delay each day was computed to estimate the period of the circadian rhythm. Results provide firm evidence that lithium can slow circadian rhythms in a mammalian system. It is suggested that lithium may either slow some circadian oscillators more than others in an organism, causing splitting, or it may interfere with internal coupling among circadian rhythms. 9 references.

001763 Kruger, Brian M.; Lavin, Paul M.; Campbell, Patrick E.; Davis, Harry N. Department of Psychology, Wright State University, Dayton, OH 45435 **Some effects of methylphenidate on self-punitive running in rats.** *Bulletin of the Psychonomic Society*. 15(3):171-174, 1980.

The effect of methylphenidate on the self-punitive running behavior of rats was evaluated. Self-punitive behavior was demonstrated in prepunishment speeds during extinction following shock escape training in a straight runway under no dose, low dose, and high dose methylphenidate conditions. Increased dosage enhanced punished running and nonpunished running. Self-punitive behavior was not affected by the drug variable. The results are interpreted as compatible with conditioned fear interpretations of self-punitive behavior but nonsupportive of cognitive interpretations. 14 references. (Author abstract modified)

001764 Ksir, Charles. University of Wyoming, Laramie, WY 82071 **Reply to Richard W. Thompson's Physiological Psychology**. 7(4):456-457, 1979.

A reply to Thompson's (1979) criticism of Ksir's (1978) attempt to replicate Thompson's study of the effects of scopolamine on tonic immobility in chickens is presented. Thompson's charges of procedural irregularities in Ksir's experiments are answered. Topics discussed include: strain differences in scopolamine action and tonic immobility in chickens, methods for pooling data across repeated trials, the development of the blood-brain barrier in chickens, and previous research on the effects of scopolamine on tonic immobility in chickens. 9 references.

001765 Kuribara, Hisashi; Tadokoro, Sakutaro. Div. of Behavioral Analysis, Behavior Research Institute, Gunma University, 3-39-22 Showa-machi, Maebashi 371 Japan **Effects of psychotropic drugs on avoidance response in rats: role of baseline performances.** *Pharmacology Biochemistry and Behavior*. 11(2):203-209, 1979.

Effects of d-amphetamine, chlorpromazine, and diazepam on the discriminated avoidance response in rats were studied with reference to levels of the behavioral baseline. After d-amphetamine, avoidance and response rates increased in all cases dose dependently. Individual changes of avoidance rates were more marked in poor performers with higher baseline response rates than in those with lower response rates. Chlorpromazine suppressed avoidance in all cases in proportion with dose. More marked changes were observed in good than in poor performers regardless of baseline response rates. After diazepam, response rates decreased in almost all cases, while avoidance rates varied depending on baseline levels. Diazepam increased avoidance rates of poor performers and decreased rates in good performers in proportion with dose. Improvement of avoidance rates was more marked in poor performers with higher baseline response rates than in those with lower rates. Results suggest that behavioral effects of psychotropics are a function of avoidance baseline levels. 32 references. (Author abstract modified)

001766 Lanson, Robert N.; Eckerman, David A.; Berryman, Robert. Psychology Department, Queens College, 120 Remsen Hall, Flushing, NY 11367 **Effects of sodium pentobarbital on matching behavior in the pigeon.** *Pharmacology Biochemistry and Behavior*. 11(2):159-164, 1979.

In a matching to sample task with five alternative stimuli, nine pigeons were exposed to four dose levels (5, 7.5, 10, 12.5 mg/kg) of sodium pentobarbital. Each drug session was alternated with a control session, and six determinations were made at each dose level. Dose response curves were obtained, and drug effects are described for position specific and stimulus specific behaviors. Results suggest that the drug effect is to weaken control by the sample stimulus and shift control to properties of the comparison stimuli. 19 references. (Author abstract modified)

001767 Le Gal La Salle, G.; Lagowska, J. Laboratoire de Physiologie nerveuse, Dept. de Neurophysiologie appliquée, C.N.R.S., F-91190 Gif-sur-Yvette, France **Amygdaloid kindling procedure reduces severity of morphine withdrawal syndrome in rats.** *Brain Research*. 184(1):239-242, 1980.

The effects of amygdaloid kindling procedure on the severity of morphine withdrawal syndrome in rats were examined. Once the experimental rats were kindled, they and the controls were made dependent on morphine. Kindled animals showed a significant reduction in occurrence and severity of some withdrawal symptoms when naloxone was administered. Evidence was provided that amygdaloid kindling causes long-lasting alterations in the mechanisms involved in morphine dependence and the absti-

nence syndrome. It is concluded that a relationship may exist between epilepsy and morphine withdrawal syndrome. 18 references.

001768 Le Gal La Salle, Gildas. Lab. de Physiologie nerveuse, Dept. de Neurophysiologie appliquee, C.N.R.S., F-91190 Gif-sur-Yvette, France **Inhibition of kindling-induced generalized seizures by aminooxyacetic acid.** Canadian Journal of Physiology and Pharmacology. 58(1):7-11, 1980.

The anticonvulsant effect of aminooxyacetic acid (AOAA) was examined on a model of experimental epilepsy (kindling) induced by daily appropriate amygdaloid stimulation in the rat. Doses were administered in fully kindled animals 3 to 4 hours before triggering a seizure. At low doses (less than 15 mg/kg) AOAA had no effect whereas at higher doses (greater than 15 mg/kg) it reduced the severity of the generalized kindled seizures in over half the cases, and even sometimes completely blocked them. An unexpected lengthening of the afterdischarge threshold was also observed in about 20% of the cases. It is suggested that since the afterdischarge threshold was shown to be unaffected by the drug, it may act on the afterdischarge propagation rather than at the focal amygdaloid level. 28 references. (Author abstract modified)

001769 Le, Anh Dung; Khanna, Jatinder M.; Kalant, Harold; LeBlanc, A. Eugene. Dept. of Pharmacology, University of Toronto, Toronto, Ontario, Canada **Effect of p-chlorophenylalanine on the acquisition of tolerance to barbital.** Canadian Journal of Physiology and Pharmacology. 58(1):12-16, 1980.

The effect of p-chlorophenylalanine (p-CPA) pretreatment on barbital tolerance in the rat as measured by motor impairment on the moving belt test was examined in two studies. In one study, the p-CPA slowed the development of tolerance without altering the acute response to the challenge dose of barbital. The second study confirmed that p-CPA slowed the development of barbital tolerance. It is concluded that the present findings provide additional support for the possibility that 5-HT may be involved in the development of tolerance to sedatives. 20 references. (Author abstract modified)

001770 Leehan, S. W.; Quadagno, D. M.; Bast, J. D. Bast: Department of Anatomy, R. L. Smith Research Center, University of Kansas Medical Center, Kansas City, KS 66103 **The effects of extrahypothalamic cycloheximide on sexual receptivity in the rat.** Hormones and Behavior. 12(3):264-268, 1979.

Cycloheximide (CHX) was injected into the medial and cortical nuclei of the amygdala and the lateral septum of steroid primed ovariectomized rats in an attempt to further elucidate the role of these extrahypothalamic areas in terms of sexual receptivity. Sexual receptivity was not inhibited. It is obvious that sex hormones exert effects on the brain other than behavioral. CHX injected into the preoptic area significantly depressed sexual receptivity, a confirmation of earlier studies. The data suggest that the amygdala and lateral septum do not have a facilitating role in the steroid induction of sexual behavior in the female rat. 12 references. (Author abstract modified)

001771 Leppik, Ilo E.; Sherwin, Allan L. Montreal Neurological Institute, Montreal, Quebec, Canada **Intravenous phenytoin and phenobarbital: anticonvulsant action, brain content, and plasma binding in rat.** Epilepsia. 20(3):201-207, 1979.

14C-phenytoin or 3H-phenobarbital were given through indwelling jugular catheters to 65 rats. Anticonvulsant activity was tested by the maximal electroshock seizure test and was correlated with brain concentrations of phenytoin or phenobarbital. Free and total plasma drug levels were determined by equilibrium dialysis. The results indicate that phenytoin is effective

in abolishing the tonic hindlimb extensor component of maximal electroshock seizures 3 min after infusion. There were marked differences in plasma protein binding characteristics of phenytoin and phenobarbital. Brain content of phenytoin exceeded the plasma free concentration 3 min after infusion. The results suggest that phenobarbital given intravenously is effective. However, the clinical problems of sedation and depression of respiratory function with phenobarbital make phenytoin a more rational choice in the acute treatment of repetitive seizures. 20 references. (Author abstract modified)

001772 Letz, Richard Errol. University of Texas at Austin **Morphine analgesia as a behavioral model for testing the opponent-process theory of motivation.** (Ph.D. dissertation). Dissertation Abstracts International. 39(11):5629-B, 1979. Ann Arbor, Univ. Microfilms No. 7910987, 98p., 1978.

Five experiments are reported which employed morphine-induced analgesia and hyperalgesia in rats to provide empirical support for the opponent process theory of motivation formulated by Solomon and Corbit. Results of these experiments provide further evidence on the role of associative processes in the display of morphine tolerance as well as support for the opponent process model. Inadequacies of Solomon's opponent process theory, Siegel's conditioned compensatory response theory of tolerance, Wikler's theory of conditioned counter adaptations, and the nature of Pavlovian conditioned responses are discussed. (Journal abstract modified)

001773 Levine, Tina E.; Erinoff, Lynda; Dregits, Duane P.; Seiden, Lewis S. Dept. of Pharmacological and Physiological Sciences, University of Chicago, 947 East 58th Street, Chicago, IL 60637 **Effects of neonatal and adult 6-hydroxydopamine treatment on random-interval behavior.** Pharmacology Biochemistry and Behavior. 12(2):281-285, 1980.

Rats were given intraventricular injections of 6-hydroxydopamine (6-HDA) or saline ascorbate vehicle as neonates (3 days old) and as adults (49 and 51 days old) and at 73 days were trained on a random interval 90 sec schedule of water reinforcement. The rats treated with 6-HDA as neonates showed response rates which were not significantly different from vehicle treated rats. Both L-Dopa and apomorphine decreased response rates at all doses tested. There were no differences among the groups with respect to the effect of these drugs. Adult treated rats showed greater response rate decreases following peripheral decarboxylase inhibition with Ro 4-4602. Catecholamine analyses revealed the rats treated with 6-HDA as neonates had greater depletions in the striatum and the remainder of telencephalon than adult treated rats but an increase in brainstem norepinephrine. These findings suggest that age at time of treatment is an important determinant of the biochemical and behavioral effects of treatment with 6-HDA. 18 references. (Author abstract)

001774 Levine, Tina E.; McGuire, Patricia S.; Heffner, Thomas G.; Seiden, Lewis S. Dept. of Pharmacological and Physiological Sciences, University of Chicago, 947 East 58th Street, Chicago, IL 60637 **DRL performance in 6-hydroxydopamine-treated rats.** Pharmacology Biochemistry and Behavior. 12(2):287-291, 1980.

Adult rats were given intraventricular injections of 6-hydroxydopamine (6-HDA) or saline ascorbate vehicle prior to exposure to a differential reinforcement of low rate (DRL) 18 sec. schedule of water reinforcement. The 6-HDA treatment did not alter the acquisition or maintenance of DRL performance despite large depletions of dopamine and norepinephrine in brain. The 6-HDA treatment completely blocked the response rate increasing effects of amphetamine but did not alter the rate decreasing effects of amphetamine on DRL performance. These

findings suggest that 6-HDA treated rats are able to respond to the contingencies necessary to maintain reinforcement on a DRL schedule. 18 references. (Author abstract)

001775 Lewis, Michael E.; Brown, Roger M.; Brownstein, Michael J.; Hart, Tessa; Stein, Donald G. Psychological Laboratory, University of Cambridge, Downing St., Cambridge CB2 3EB, England **Nerve growth factor: effects on d-amphetamine-induced activity and brain monoamines.** *Brain Research.* 176(2):297-310, 1979.

Brain monoamine levels and behavioral responses to d-amphetamine were determined in male Sprague-Dawley rats 15 days after 6-hydroxydopamine lesions of the nucleus accumbens and injections of saline and or nerve growth factor (NGF) near the substantia nigra. The locomotor response to d-amphetamine (1.5mg/kg) was enhanced in NGF treated rats, compared to controls. Levels of dopamine and norepinephrine (NE) in the striatum and nucleus accumbens were depressed equally in the NGF and saline groups, indicating the apparent recovery of the NGF treated rats was not due to catecholaminergic neuronal re-growth. Intracerebral NGF also enhanced the response to d-amphetamine 15 days later in intact rats and increased turnover of brain NE and serotonin at 3 but not 15 days after administration. Results indicate that intracerebral NGF can produce similar behavioral changes in brain-damaged and intact rats and can modify the apparent turnover of brain monoamines. 56 references. (Author abstract modified)

001776 Lien, Eric J.; Liao, Richard C. H.; Shinouda, H. G. Section of Biomedical Chemistry, School of Pharmacy, University of Southern California, Los Angeles, CA 90033 **Quantitative structure-activity relationships and dipole moments of anticonvulsants and CNS depressants.** *Journal of Pharmaceutical Sciences.* 68(4):463-465, 1979.

A quantitative analysis of the structure/activity relationships of 16 commercially available anticonvulsant drugs is presented. Equations correlating anticonvulsant activities with physicochemical constants were formulated. For the maximal electroshock seizure test and the pentylenetetrazol seizure threshold test, good correlations were obtained only when diazepam, clonazepam, and carbamazepam were not included. All 16 compounds could be included in a single equation for the median toxic dose/rotorod ataxia test. The dipole moments of seven clinically used antiepileptic drugs were measured in 1,4-dioxane. 14 references. (Author abstract modified)

001777 Lineberry, Charles G.; Kulics, Albert T. Medical Division, Burroughs Wellcome Co., 3030 Cornwallis Rd., Research Triangle Park, NC 27709 **Morphine effects on escape in the rhesus monkey.** *Neuropharmacology.* 19(1):107-110, 1980.

The effects of morphine (0.5, 1.0, and 2.0mg/kg) on escape from noxious electrical cutaneous shock were determined in three male rhesus monkeys. Morphine reduced escape responding in two Ss and increased responding in one. Data analysis by signal detection theory (SDT) showed that stimulus sensitivity was increased in two Ss and reduced in one. Results indicate that the effects of morphine, like those of diazepam, vary qualitatively across subjects. SDT may be of limited value for assessing narcotic analgesia, since it does not discriminate between narcotic and anti-anxiety drugs. 8 references. (Author abstract modified)

001778 Lockard, Joan S.; Levy, Rene H.; Congdon, William C.; DuCharme, Larry L.; Salonen, Leonard D. Dept. of Neurological Surgery, University of Washington, Seattle, WA 98195 **Clonazepam in a focal-motor monkey model: efficacy, tolerance, toxicity, withdrawal, and management.** *Epilepsia.* 20(6):683-695, 1979.

An alumina gel monkey model was used to evaluate quantitatively the efficacy of clonazepam (CZP) in focal/motor seizures. Two groups of monkeys were given CZP in polyethylene glycol 400 (PEG) or a PEG solution alone for 6 weeks; treatments were bordered at both ends by 3 weeks of saline treatment to establish a baseline. Results indicate the CZP is effective for focal/motor seizures and secondarily generalized tonic/clonic seizures, particularly when its concentration in plasma is higher than 60ng/ml. Withdrawal seizures were evident on cessation of CZP administration. CZP is concluded to be a useful broad spectrum anticonvulsant when managed carefully. Cessation of PEG administration was unexpectedly found to reduce seizure frequency in subsequent weeks to a level below the initial baseline level. 17 references. (Author abstract modified)

001779 Lorden, Joan F.; Callahan, Michael; Dawson, Ralph, Jr. Dept. of Psychology, University of Alabama in Birmingham, Birmingham, AL 35294 **Depletion of central catecholamines alters amphetamine- and fenfluramine-induced taste aversions in the rat.** *Journal of Comparative and Physiological Psychology.* 94(1):99-114, 1980.

The attenuation of conditioned taste aversions induced by pairing the consumption of saccharin with an amphetamine injection in rats with depletion of central catecholamines caused by intraventricular administration of 6-hydroxydopamine (6-OHDA) was investigated. The hypothesis that dopamine (DA) depletion is responsible for this effect was tested. The reduction in conditioning caused by intraventricular 6-OHDA could not be duplicated either with injections of 6-OHDA into the substantia nigra or with intraventricular 6-OHDA injections in animals pretreated with desmethylimipramine. Both treatments, however, produced large depletions of telencephalic DA. 6-Hydroxydopa infusions caused a preferential loss of telencephalic norepinephrine (NE) but also failed to alter taste aversion learning. It is concluded that the effect of intraventricular 6-OHDA on amphetamine-induced aversions was the result of depletion of both NE and DA. In another experiment, the generality of the effect was examined by pairing saccharin consumption with injections of the amphetamine congener fenfluramine. Depletion of both NE and DA failed to alter fenfluramine-induced aversions. Infusion of 6-OHDA into the substantia nigra, however, retarded the extinction of such an aversion. Evidence is discussed for a peripheral site of action for fenfluramine in the conditioned aversion paradigm. 56 references. (Author abstract modified)

001780 Lucki, I.; Harvey, J. A. Dept. of Psychology, University of Iowa, Iowa City, IA 52242 **Increased sensitivity to d- and l-amphetamine action after midbrain raphe lesions as measured by locomotor activity.** *Neuropharmacology.* 18(3):243-249, 1979.

The effects of d-amphetamine and l-amphetamine on locomotor activity and stereotyped behavior were studied in intact rats and in rats with lesions of the raphe nuclei (RN) or dorsolateral tegmentum (DLT). The RN lesions produced a large (93%), selective depletion of serotonin in the telencephalon and enhanced the effects of both amphetamine isomers on locomotor activity. The median effective dose for the motor stimulatory effects of amphetamine was reduced to about one third of control values in the RN lesioned rats. RN lesions significantly increased the maximum levels of locomotor responding to d-amphetamine, but not to l-amphetamine. Rats with RN lesions showed a significantly greater incidence of stereotyped behavior at a low dose of d-amphetamine than did controls. The DLT lesions produced a selective but small (54%) decrease in telencephalic content of norepinephrine and had no effect on the actions of amphetamine. 29 references. (Author abstract modified)

001781 Mactutus, Charles F.; Smith, Robert L.; Riccio, David C. Riccio: Dept. of Psychology, Kent State University, Kent, OH 44242 **Extending the duration of ACTH-induced memory reactivation in an amnesia paradigm.** *Physiology & Behavior*. 24(3):541-546, 1980.

The effectiveness of ACTH treatment in reversing hypothermia-induced retrograde amnesia was investigated in a passive avoidance paradigm using 27 adult male Holtzman albino rats. Subcutaneous injections of ACTH 30 minutes prior to a retention test attenuated the amnesia typically evidenced 24 hours after whole body cooling. When ACTH was combined with brief exposure to the fear cues previously associated with training substantial memory recovery was sustained over 24 hours. Another experiment suggested that the memory recovery induced by the combined ACTH/cue exposure persisted over 7, but not 14 days. It is suggested that although the combined hormone/behavioral reactivation treatment may extend the duration of ACTH-induced recovery from amnesia, a reactivated memory, like other memories, appears susceptible to ordinary sources of retention loss. 33 references. (Author abstract modified)

001782 Maes, Hugo. Laboratorium voor Neuro- en Psychofysiologie, Katholieke Universiteit Leuven, Campus Gasthuisberg, Herestraat, B-3000 Leuven, Belgium **Feeding, scanning and photophobia after local injection of pentobarbital or noradrenaline into the ventromedial hypothalamus.** *Behavioural Processes*. 4(3):239-252, 1979.

Effects of injection of pentobarbital or noradrenaline into the ventromedial hypothalamus (VMH) of ad libitum fed male Wistar rats were investigated. Such injections promptly but transiently elicited feeding behavior. No conspicuous differences were found between the effects of the two VMH interventions of behavior elements such as grooming, sniffing, and locomotion. Scanning, however, was clearly depressed upon microinjection with pentobarbital. Subsequently, VMH application of pentobarbital but not of noradrenaline was found to mitigate the animals' spontaneous aversion towards brightly illuminated areas. Therefore, it is tentatively suggested that the VMH contains a network for feeding and another nonnoradrenergic one for responsiveness towards novel and fearful environmental stimuli. 38 references. (Author abstract modified)

001783 Mailman, R. B.; Ferris, R. M.; Tang, F. L. M.; Vogel, R. A.; Kiltz, C. D.; Lipton, M. A.; Smith, D. A.; Mueller, R. A.; Breese, G. R. Biological Sciences Research Center, University of North Carolina, Chapel Hill, NC 27514 **Erythrosine (red no. 3) and its nonspecific biochemical actions: what relation to behavioral changes?** *Science*. 207(4430):535-537, 1980.

Recent studies of the effect of erythrosine (red food dye number 3) on neurotransmitter uptake are reviewed within the context of a series of replications and extensions. Biochemical studies have shown that the ability of erythrosine to inhibit dopamine (DA) uptake into brain synaptosomal preparations is dependent on the concentration of tissue present in the assay mixture. Thus the finding of erythrosine inhibition of DA uptake (which if true could provide a plausible explanation of the Feingold hypothesis of childhood hyperactivity) may simply be an artifact resulting from nonspecific interactions with brain membranes. Although erythrosine given parenterally (50mg/kg) did not alter locomotor activity of control of 6-hydroxydopamine treated rats, erythrosine (50 to 300mg/kg) attenuated the effect of punishment in a conflict paradigm. 24 references. (Author abstract modified)

001784 Mangiapane, Michael L.; Simpson, John B. Dept. of Psychology, University of Washington, Seattle, WA 98195

Pharmacologic independence of subfornical organ receptors mediating drinking. *Brain Research*. 178(2-3):507-517, 1979.

The relationship between cholinergic and angiotensin (AII) induced drinking was investigated pharmacologically in male Long-Evans rats with chronically implanted cannulae in the subfornical organ. Intracranial injection of low doses of the muscarinic antagonist atropine abolished carbachol-induced drinking, but a large dose of atropine had no effect on AII-induced drinking. Nicotinic antagonists had no effect. Small doses of the AII antagonist saralasin blocked AII-induced drinking, but a large dose had no effect on carbachol-induced drinking. Results indicate that the receptors mediating cholinergic and AII-induced drinking exist in parallel rather than in series. 33 references. (Author abstract modified)

001785 Marçais, H.; Protais, P.; Costentin, J. UER de Médecine et de Pharmacie, Laboratoire de Pharmacodynamie et de Physiologie, 49, rue du Maulevrier, F-76000 Rouen, France **Hypersensitivity of the climbing behaviour response to apomorphine induced by a short depression of dopaminergic neurone activity.** *Neuropharmacology*. 18(11):845-849, 1979.

The climbing behavior elicited by apomorphine was enhanced in male Swiss mice pretreated with drugs known to depress the firing rate of dopaminergic neurons (gamma-hydroxybutyrate, 350mg/kg; gamma-butyrolactone, 750mg/kg; or baclofen, 20mg/kg). The hyperresponsiveness to apomorphine was evident as soon as the acute effects of these drugs wore off (3 to 6 hours), persisted for 2 to 3 days, and could be prevented by inhibition of protein synthesis. The enhanced response to apomorphine was similar in many ways to hypersensitivity induced by other treatments that interrupt striatal dopaminergic transmission. 41 references. (Author abstract modified)

001786 Marshall, John F. Dept. of Psychobiology, University of California, Irvine, CA 92717 **Somatosensory inattention after dopamine-depleting intracerebral 6-OHDA injections: spontaneous recovery and pharmacological control.** *Brain Research*. 177(2):311-324, 1979.

Unilateral injection of 6-hydroxydopamine into the area ventralis tegmenti of male Sprague-Dawley rats pretreated with desmethylimipramine resulted in an inattention to somatosensory stimuli impinging on the contralateral body surface. Seven rats showed no recovery of orientation to touch during 4 postoperative months, eight showed marked loss of orientation followed by nearly complete recovery within 1 month, and eleven showed only a minimal deficit in orientation. In rats that did recover, orientation to touch recovered first in rostral body points. Low doses of alpha-methyl-p-tyrosine or spiroperidol to rats that had spontaneously recovered from the somatosensory inattention syndrome reinstated contralateral inattention without affecting orientation to ipsilateral touch; orientation was affected in a caudal to rostral direction as the drugs took effect and recovered in rostrocaudal direction. Neostriatal dopamine was highly correlated with the extent of somatosensory orientation observed immediately after surgery and during the postoperative month. 21 references. (Author abstract modified)

001787 Martinez, J. L., Jr.; Jensen, R. A.; Messing, R. B.; Vasquez, B. J.; Soumireu-Mourat, B.; Geddes, D.; Liang, K. C.; McGaugh, J. L. Dept. of Psychobiology, School of Biological Sciences, University of California, Irvine, CA 92717 **Central and peripheral actions of amphetamine on memory storage.** *Brain Research*. 182(1):157-166, 1980.

The effects of posttraining administration of d-amphetamine on retention of a one trial inhibitory avoidance response were determined in male Sprague-Dawley rats. Retention was enhanced by peripheral administration of amphetamine (1.0mg/kg i.p.) im-

mediately after training, but intracerebroventricular administration of the drug in doses from 50 to 500mcg did not alter retention. In rats given peripheral 6-hydroxydopamine 24 hours before training, a lower peripheral dose of amphetamine (0.25mg/kg) was most effective in enhancing retention. Results suggest that the memory enhancing effects of D-amphetamine are mediated at least in part through peripheral systems. 25 references. (Author abstract modified)

001788 Mason, Stephen T.; Fibiger, Hans C. Division of Neurological Sciences, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Noradrenaline and selective attention.** *Life Sciences*. 25(23):1949-1956, 1979.

Rats depleted of forebrain noradrenaline by intracerebral injection of 4mcg of 6-hydroxydopamine into the dorsal noradrenergic bundle were examined on their ability to ignore irrelevant stimuli. In the latent inhibition paradigm, normal rats were preexposed to visual and auditory stimuli in the absence of reward; such preexposure was found to slow subsequent learning of a successive discrimination task using these stimuli. Noradrenaline depletion blocked the usual latent inhibition effect, thus suggesting that the lesioned animals were impaired in ignoring irrelevant stimuli. As second paradigm, a nonreversal shift, involved training rats on a two dimensional discrimination task with one dimension relevant and the other irrelevant. Nonreversal shift (in which the initially irrelevant dimension became the sole relevant one) was significantly improved by 6-hydroxydopamine lesion. It is concluded that strong evidence has been presented in favor of a role for the dorsal noradrenergic bundle in attentional filtering processes. 28 references. (Author abstract)

001789 Masuda, Y.; Utsui, Y.; Shiraishi, Y.; Karasawa, T.; Yoshida, K.; Shimizu, M. Research Laboratories, Daiippon Pharmaceutical Co., Ltd., Suita-shi, Osaka 564, Japan **Relationships between plasma concentrations of diphenylhydantoin, phenobarbital, carbamazepine, and 3-sulfamoylmethyl-1,2-benzisoxazole (AD-810), a new anticonvulsant agent, and their anticonvulsant or neurotoxic effects in experimental animals.** *Epilepsia*. 20(6):623-633, 1979.

The relationships between plasma concentrations of diphenylhydantoin (DPH), phenobarbital (PB), carbamazepine (CBZ), and 3-sulfamoylmethyl-1,2-benzisoxazole (AD-810), a new anticonvulsant agent, and their anticonvulsant and neurotoxic effects were studied in mice, rats, rabbits, dogs, and monkeys. It was demonstrated that both the anticonvulsant effects and the neurotoxic effects of the drugs tested were more closely correlated with their plasma concentrations than with the dosages administered. A critical plasma concentration for anticonvulsant and neurotoxic effects of each drug was found to be relatively constant among different species, with the exception of DPH in rabbits. The therapeutic ranges of plasma concentrations of DPH, PB, and CBZ determined in various species of animals coincided well with those recommended clinically. AD-810 was found to be effective against maximal electroshock seizure without signs of neurological toxicity in ranges of plasma concentrations reported for each species of animal. 36 references. (Author abstract modified)

001790 Matte, Alexander C. Dept. of Neurology, University Hospital Eppendorf, D-2000 Hamburg 20, Germany **Biphasic and dissociated effects of ACTH on motor activity, aggression and Psychoneuroendocrinology.** 4(1):21-27, 1979.

Aggressive behavior, motor activity, and defecation were examined simultaneously in male wild mice treated daily with adrenocorticotrophic hormone (ACTH). Aggression increased on days 1 through 4 of ACTH treatment, but decreased during days 4 through 7. Motor activity not associated with aggressive

behavior was decreased by ACTH, as was defecation. 51 references. (Author abstract modified)

001791 Matthews, R. T.; Chiou, C. Y. Dept. of Pharmacology, University of Texas Southwestern Medical Center, Dallas, TX 75235 **Effects of acute and chronic injections of carbachol in the rat caudate nucleus.** *Neuropharmacology*. 18(3):291-294, 1979.

Contralateral forelimb tremors were recorded in male rats given unilateral injections of carbachol into the caudate nucleus once a week for 3 weeks. Most animals showed a decrease in tremor amplitude and duration by the third week, but the group mean values were not significantly lower than those in the first week. Tremor onset latency and the frequency of other drug-induced behavioral effects did not change. Tolerance to the effects of carbachol was observed in rats given continued weekly injections. A 4.5 week rest period was required for complete return of tremors. 11 references. (Author abstract modified)

001792 Matthews, W. D.; McCafferty, G. P. Dept. of Biological Research, Smith Kline & French Laboratories, Philadelphia, PA 19101 **Anticonvulsant activity of muscimol against seizures induced by impairment of GABA-mediated neurotransmission.** *Neuropharmacology*. 18(11):885-889, 1979.

The effect of the GABA agonist muscimol on seizures induced in male Sprague-Dawley rats by agents that impair GABA mediated neurotransmission was examined. Muscimol delayed the onset of isoniazid and picrotoxin-induced convulsions and abolished the tonic forelimb extension component of seizures induced by bicuculline and metrazole. The decreasing order of potency in inhibiting tonic forelimb extension was diazepam, muscimol, phenobarbital, phenytoin. Muscimol had no effect on strychnine-induced convulsions. It is concluded that muscimol penetrates rat brain and specifically antagonizes seizures caused by GABA receptor blockade or depletion of brain GABA. 24 references. (Author abstract modified)

001793 McCarty, Richard; Kopin, Irwin J. Kopin: Laboratory of Clinical Science, NIMH, Building 10, Room 2D-46, Bethesda, MD 20205 **Stress-induced alterations in plasma catecholamines and behavior of rats: effects of chlorisondamine and bretylium.** *Behavioral and Neural Biology*. 27(3):249-265, 1979.

The response of the sympathetic nervous system and the adrenal medulla was examined in rats subjected to the stress of handling and transfer to a shock chamber and of 5 min of intermittent footshock. The results indicate that the adrenal medulla of rats is a significant source of circulating norepinephrine during mildly and intensely stressful stimulation (approximately 33% and 45%, respectively). Further activity during footshock stress was greater in rats with an intact sympathetic nervous system than in Ss treated with bretylium or a ganglionic blocking agent (chlorisondamine). The presence of epinephrine in the circulation did not have a significant effect on the activity of rats during stress. 68 references. (Author abstract modified)

001794 McCarty, Richard; Chueh, Chuang C.; Kopin, Irwin J. Kopin: Laboratory of Clinical Science, NIMH, Building 10, Room 2D-46, Bethesda, MD 20205 **Differential behavioral responses of spontaneously hypertensive (SHR) and normotensive (WKY) rats to d-amphetamine.** *Pharmacology Biochemistry and Behavior*. 12(1):53-59, 1980.

Behavioral responses of spontaneously hypertensive (SHR) and Wistar-Kyoto (WKY) normotensive rats to d-amphetamine were compared. Animals were tested at a young age (6 weeks) to minimize the effects of elevated blood pressure on drug responsiveness. SHR rats were more active than WKY rats after injections of 1.0, 2.0, and 4.0mg/kg d-amphetamine. A significant strain difference in stereotypy was also noted; rearing oc-

curred in SHR rats while lateral or vertical head movements (head waving) occurred in WKY rats. The lack of significant strain differences in the behavioral responses of rats to apomorphine, a direct acting dopamine agonist, suggested that the differential behavioral responses to d-amphetamine were not a result of differences between strains in receptor sensitivity. Pretreatment of rats with reserpine eliminated the strain differences in behavioral responses to d-amphetamine. Pretreatment of rats with alpha-methyl-p-tyrosine prior to administration of d-amphetamine eliminated the strain differences in stereotyped behavior; however, WKY rats remained less active than SHR rats. Pretreatment of SHR rats with parachlorophenylalanine had no effect on the behavioral responses to d-amphetamine. In contrast, pretreatment of WKY rats with parachlorophenylalanine resulted in an increase in rearing and a decrease in head waving following an injection of d-amphetamine. These findings suggest that the differences in responses to d-amphetamine of SHR and WKY rats are due in part to variations in the activities of central catecholaminergic and serotonergic neurons. 55 references. (Author abstract)

001795 McCown, Thomas J.; Barrett, Robert J. Tennessee Neuropsychiatric Institute, 1501 Murfreesboro Road, Nashville, TN 37217 Development of tolerance to the rewarding effects of self-administered S(+)amphetamine. *Pharmacology Biochemistry and Behavior*. 12(1):137-141, 1980.

The development of tolerance to the rewarding effects of self-administered S(+)amphetamine (AMPH) was investigated. Rats were implanted with chronic intravenous cannulae and trained to bar-press intravenous, self-administered AMPH. After establishment of a for steady baseline at 0.25mg/kg/reinforcement, the animals were removed from the test situation and subsequently injected three times a day for 4 days with increasing amounts of AMPH (total of 78mg/kg). Thirty-six hours after the last injection, the animals were tested for tolerance to self-administered AMPH, and all the animals increased the amount of drug intake by at least 45% over baseline. The brain disappearance of a 10mg/kg i.v. dose of AMPH was measured for the chronic AMPH and saline treated Ss to test for the possibility of enzyme induction. No differences were found. These data indicate that drug self-administration in rats is a useful paradigm to study tolerance to the rewarding effects of AMPH and may be useful in understanding the mechanisms mediating the mood elevating properties of the drug observed in humans. 15 references. (Author abstract modified)

001796 McDermott, Lois J.; Grossman, Sebastian P. Grossman: Dept. of Behavioral Sciences, University of Chicago, 5848 S. University Ave., Chicago, IL 60637 Responsiveness to 2-deoxy-D-glucose and insulin in rats with rostral zona incerta lesions. *Physiology & Behavior*. 24(3):585-592, 1980.

Responsiveness to 2-deoxy-D-glucose (2DG) and insulin in rats with rostral zona incerta (ZI) lesions was examined with male albino Sprague-Dawley rats. ZI lesions impaired or abolished the feeding response to a broad range of doses of 2DG, including some that were clearly subthreshold in controls as well as others that induced severe side-effects. In contrast, ZI lesions had little effect on the feeding response to a broad range of doses of insulin. It is concluded that the relatively minor effects of ZI lesions on the feeding response to insulin but not the devastating impairment of the response to 2DG may be related to the transient debilitating effects that ZI lesions had on postsurgical ad lib intake and body weight. 32 references. (Author abstract modified)

001797 McGaugh, James L.; Gold, Paul E.; Handwerker, Mark J.; Jensen, Robert A.; Martinez, Joe L.; Meligeni, John A.; Vasquez, Beatriz J. Department of Psychobiology, University of

California, Irvine, CA 92717 Altering memory by electrical and chemical stimulation of the brain. In: Brazier, M., Brain mechanisms in memory and learning. New York, Raven Press, 1979. (p. 151-164).

Recent studies examining the effects on retention of posttraining administration of electrical brain stimulation, hormones, and drugs affecting catecholamines are reviewed. The findings, in general, provide strong evidence that memory storage processes are time dependent. Both retrograde amnesia and retrograde enhancement of memory can be produced by posttraining treatments. The fact that retrograde enhancement and disruption of memory is produced by treatments affecting substances ordinarily released when animals are stimulated provides support for the view that such substances serve to modulate neuronal processes underlying memory. It is suggested that further study of the ways in which posttraining treatments influence adrenocorticotrophic hormones and monoamines as well as the ways in which hormones affect neuronal activity should provide some important leads to understanding how the brain acts to store experiences. 56 references.

001798 McGeer, P. L.; McGeer, E. G.; Campbell, J. J. R. Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver, British Columbia, V6T 1W5 Canada Rotatory effects of intracerebral tetanus toxin injections. *Experimental Neurology*. 67(2):363-367, 1980.

Data which indicates that the ipsilateral turning produced by nigral injections is probably not mediated by the dopaminergic system is presented. Injection of tetanus toxin into the substantia nigra or thalamus of rats produced almost immediately marked ipsilateral turning. Injection into the caudate led to similar turning, delayed 3 to 5 days in onset. It is concluded that the available data suggest that the effects were not mediated by the dopaminergic system. 12 references. (Author abstract modified)

001799 McGinnis, Marilyn Y.; Gordon, John H.; Gorski, Roger A. Rockefeller University, New York, NY 10021 Influence of gamma-aminobutyric acid on lordosis behavior and dopamine activity in estrogen primed spayed female rats. *Brain Research*. 184(1):179-191, 1980.

The role of gamma-aminobutyric acid (GABA) in the display of lordosis behavior in estrogen primed spayed female rats was examined. Picrotoxin, which blocks GABA receptors, was effective in suppressing the high levels of lordosis behavior seen in the estradiol benzoate (EB) primed septal lesioned female 30 minutes after infusion, but not at 120 min. Conversely, hydrazonepropionic acid (HPA), which elevates endogenous GABA levels, was effective in facilitating lordosis behavior in sham operated rats treated with EB only. Sham operated rats receiving HPA infusions had lower dopamine and homovanillic acid levels compared to those of saline injected controls, and septal lesioned rats receiving picrotoxin infusions had higher dopamine and homovanillic acid levels than those of lesioned saline injected controls. It is concluded that these results support the concept of a GABA inhibitory neuronal feedback system which modulates dopamine turnover and perhaps plays a critical role in the neural control of lordosis behavior. 33 references. (Author abstract modified)

001800 McGinnis, Marilyn Y.; Gorski, Roger A. Dept. of Anatomy, UCLA School of Medicine, Los Angeles, CA 90024 Sexual behavior of male and female septal lesioned rats. *Physiology & Behavior*. 24(3):569-573, 1980.

The sexual behavior of male and female gonadectomized rats with septal lesions or sham operations was examined. Females were tested for lordosis behavior after daily injections of estradiol benzoate (EB) for 3 days, while males were tested after EB

only, and after EB plus progesterone (PROG). The mean lordosis quotients of septal lesioned female rats were higher than those of sham operated controls. No increase in lordosis responding was seen in male rats with either EB alone or EB plus PROG. It is concluded that the increased hormone sensitivity is specific for lordosis behavior, at least when the septal lesions are given in adulthood. 17 references. (Author abstract modified)

001801 McMillan, D. E. Dept. of Pharmacology, School of Medicine, University of Arkansas for Medical Sciences, 4301 West Markham St., Little Rock, AR 72201 **Effects of d-amphetamine and caffeine on schedule-controlled and schedule-induced responding.** *Journal of the Experimental Analysis of Behavior.* 32(3):445-456, 1979.

The effects of d-amphetamine and caffeine were studied in rates and patterns of rat lever-pressing and schedule-induced licking under a multiple fixed-ratio (FR) fixed-interval (FI) schedule. Caffeine reduced mean overall rates of licking at lower doses than it reduced mean overall rates of lever-pressing under the FI schedules, but the effects on licking and lever-pressing depended largely on the control rate of responding. D-amphetamine reduced mean overall rate of lever-pressing and licking at about the same dose, but its effects also were a function of the control rate of responding. 19 references. (Author abstract)

001802 Meinkoth, J.; Quadagno, D. M.; Bast, J. D. Quadagno: Department of Physiology and Cell Biology, University of Kansas, Lawrence, KS 66045 **Depression of steroid-induced sex behavior in the ovariectomized rat by intracranial injection of cycloheximide: preoptic area compared to the ventromedial hypothalamus.** *Hormones and Behavior.* 12(3):199-204, 1979.

The effect of three doses of cycloheximide (CHX) into the preoptic area or ventromedial hypothalamus on steroid-induced sexual receptivity in the ovariectomized estrogen primed rat was compared. Sexual receptivity was significantly depressed after the bilateral injection of 5mcg, 10mcg, or 20mcg 6 hours before the initiation of the steroid priming. There was no differential response to CHX, an inhibitor of protein synthesis, relative to the locus of the placement of the drug in either the preoptic area or ventromedial hypothalamus. 10 references. (Author abstract modified)

001803 Mendelson, Wallace B.; Gillin, J. Christian; Piser, Gary; Wyatt, Richard J. Building 10, Room 3N224, NIH, Bethesda, MD 20205 **Arginine vasotocin and sleep in the rat.** *Brain Research.* 182(1):246-249, 1980.

The effects of arginine vasotocin (AVT, 0.5 mcg/kg to 50mcg/kg i.p.) on sleep and behavior were examined in male Sprague-Dawley rats. Low doses of AVT had no apparent effects, but the 50mcg/kg dose reduced REM latency by 65% without altering sleep latency, total sleep, or total amount of REM in the first 2 hours. No significant toxic effects were evident in tests for cataplexy, equilibrium, and righting, grasping, and tail pinch reflexes. 10 references.

001804 Messiha, F. S. Dept. of Pathology, Texas Tech University School of Medicine, Lubbock, TX 79430 **Taurine, analogues and ethanol elicited responses.** *Brain Research Bulletin.* 4(5):603-607, 1979.

The effects of taurine and related compounds on spontaneous motor activity in male Sprague-Dawley mice and on ethanol mediated responses in rats were determined. Taurine (50mg/kg i.p.) did not significantly alter motor activity in mice, but behavioral depression was apparent after injection of 50mg/kg cysteine hydrochloride or taurocholic acid. Administration of taur-

ocholic acid (50mg/kg i.p.) 30 minutes prior to a narcotic dose of ethanol (5g/kg i.p.) reduced the time required for the onset of ethanol narcosis, and pretreatment with cysteine acid (50mg/kg i.p.) prolonged ethanol narcosis. Treatment with cysteine acid 30 minutes prior to 2.5g/kg ethanol decreased whole blood ethanol concentrations without altering brain ethanol levels. Taurocholic acid (100mg/kg i.p.) decreased the intake of an ethanol solution in rats preferring 5% ethanol solution over water. None of the compounds tested altered endogenous specific activity of mouse liver alcohol dehydrogenase when given one once daily for 10 consecutive days. Results suggest that taurocholic acid and cysteine acid exert additive action to some ethanol elicited responses. 15 references. (Author abstract modified)

001805 Messing, R. B.; Jensen, R. A.; Martinez, J. L., Jr.; Spiehler, V. R.; Vasquez, B. J.; Soumireu-Mourat, B.; Liang, K. C.; McGaugh, J. L. Dept. of Psychobiology, School of Biological Sciences, University of California, Irvine, CA 92717 **Naloxone enhancement of memory.** *Behavioral and Neural Biology.* 27(3):266-275, 1979.

Evidence is presented that naloxone enhances retention when systemically administered to male F344 rats after training in a one trial inhibitory avoidance task. The memory enhancing ability to naloxone appears to be opiate receptor dependent because it was antagonized by morphine. Naloxone also improved retention of rats in an active avoidance task, indicating that the effect is not task specific. The influence on retention was time dependent in both tasks. The drug must be present for a considerable period beginning soon after the onset of memory consolidation in order to be effective. For inhibitory avoidance, it must be administered immediately after training and again 30 min later. Naloxone is effective in the active avoidance task only when given both immediately before and within 30 min after the eight acquisition trials. It is concluded that naloxone influences memory and that endogenous opioid systems are involved in memory storage processes. 22 references. (Author abstract modified)

001806 Michanek, A. Dept. of Medical Pharmacology, University of Uppsala, Uppsala, Sweden **Potentiation of D- and L-amphetamine effects on copulatory behavior in female rats by treatment with alpha-adrenoreceptor blocking drugs.** *Archives Internationales de Pharmacodynamie et de Therapie.* 239(2):241-256, 1979.

The alpha-adrenergic receptor blockers phenoxybenzamine, phentolamine, and prazosin potentiated the inhibitory effect of d-amphetamine on lordosis behavior in ovariectomized female Sprague-Dawley rats treated with estrogen and progesterone. Phenoxybenzamine and prazosin also potentiated the effect of l-amphetamine on lordosis behavior in these animals, but phentolamine did not. Pretreatment with phenoxybenzamine or phentolamine failed to augment the effect of amphetamine on stereotyped activity. L-propranolol, a beta-adrenergic receptor blocker, and pimozide, a dopamine receptor blocker, did not alter the effects of amphetamine on lordosis behavior. Clonidine, an alpha-adrenergic receptor stimulant, inhibited the lordosis response in estrogen treated rats, probably via a presynaptic mechanism. It is suggested that amphetamine activates a noradrenergic system that influences lordosis behavior by direct facilitation or by decreasing the activity of an inhibitory serotonergic system. 41 references. (Author abstract modified)

001807 Mickley, G. Andrew; Teitelbaum, Herman. Dept. of Behavioral Sciences and Leadership, USAF Academy, Colorado Springs, CO 80840 **Yohimbine blocks lateral hypothalamus-mediated behaviors.** *European Journal of Pharmacology.* 60(2/3):143-151, 1979.

Male Sprague-Dawley rats treated with yohimbine showed active avoidance performance deficits similar to those seen in rats with lateral hypothalamic lesions. Systemic injections of yohimbine caused decrements in lateral hypothalamic self-stimulation behaviors and in locomotor activity induced by lateral hypothalamic stimulation; similar behaviors mediated by the substantia nigra were not significantly altered by yohimbine. Yohimbine also reduced the enhanced glucose utilization normally observed in the lateral hypothalamus during electrical stimulation. 32 references. (Author abstract modified)

001808 Misantone, Louis J.; Ellis, Susan; Epstein, Alan N. Dept. of Anatomy, Philadelphia College of Osteopathic Medicine, 4150 City Line Avenue, Philadelphia, PA 19131 **Development of angiotensin-induced drinking in the rat.** *Brain Research*. 186(1):195-202, 1980.

The effects of angiotensin on the drinking behavior of the neonatal rat were investigated. The suckling rat was found to respond from birth to intraventricular angiotensin, and the drinking behavior elicited by the hormone achieved adult characteristics of reliability and sensitivity at 4 to 5 days of age. Additional testing of 5-day-old rats injected with a range of doses showed that the threshold dose lies between 0.1 to 1.0mg, which is comparable to the adult sensitivity to intraventricular injections. The hormone also increased milk intake in neonates, but the animals chose water over milk as early as 17 days. The results are discussed in terms of the neuropsychological and neuroendocrinological systems for several major forms of thirst. 15 references. (Author abstract modified)

001809 Modrow, Harold E.; Bliss, David K. Bliss: Scholl of Medicine, Southern Illinois University, Carbondale, IL 62901 **Electrophysiological correlates of state-dependent learning.** *Physiological Psychology*. 7(3):259-262, 1979.

Electrophysiological changes taking place during learning and recall in a state dependent paradigm were examined. Male Sprague-Dawley rats were implanted with recording electrodes in both the mesencephalic reticular formation (MRF) and the anterior polysensory cortex. After recovery, they were trained in a state dependent learning paradigm utilizing a two way shuttle avoidance procedure. The animals trained under 15mg/kg sodium pentobarbital learned the task faster than the saline trained animals. Both recording sites showed a frequency difference between avoidance trials and error trials. After criterion was reached, the animals were given overtraining trials. It was found that transfer to the opposite drug state was related positively to the amount of overtraining given. The MRF frequency in the test situation showed a difference between trials in which there was a response and those in which there was not. These results are discussed in relation to John's hypothesized circuits mediating the retrieval of memory. 20 reference. (Author abstract modified)

001810 Moerschbaecher, Joseph M.; Thompson, Donald M.; Thomas, John R. Department of Pharmacology, Georgetown University Schools of Medicine and Dentistry, Washington, DC 20007 **Effects of methamphetamine and scopolamine on variability of response location.** *Journal of the Experimental Analysis of Behavior*. 32(2):255-263, 1979.

Methamphetamine and scopolamine were studied in monkeys responding under a fixed-ratio/fixed-interval schedule of reinforcement. Variability of response location was evaluated in terms of switches, where a switch was defined as a response on one lever followed by a response on a different lever. Under baseline conditions the fixed-ratio schedule generated a high rate of responding and a low level of variability, while the fixed-interval schedule generated a low rate of responding and a high

level of variability. Both methamphetamine and scopolamine decreased overall response rate and increased variability of response location in each component of the multiple schedule with increasing doses of drug. It is reported that at lower doses both drugs were found to decrease rate without affecting response variability. 28 references. (Author abstract modified)

001811 Mollenauer, Sandra; White, Michael; Plotnik, Rod; Tiffany, P. Bradley. Dept. of Psychology, San Diego State University, San Diego, CA 92182 **Physostigmine: effects on fear or defense responses in the rat.** *Pharmacology Biochemistry and Behavior*. 11(2):189-195, 1979.

The effects of the anticholinesterase, physostigmine, were investigated on fear and defense responses in the rat. Physostigmine caused an increase in the defense responses of male hooded rats. Physostigmine caused significantly more freezing and significantly more suppression of feeding and of time near the versive stimulus. Dose response curves showed a positive linear relationship between dose (0.025, 0.05, 0.1, and 0.2mg/kg) and defense responses. Results could not be attributed to general response suppression since the drug effects were situation specific. Results are taken as further evidence of the involvement of cholinergic activity in the mediation of observable defense responses and are thought to have important implications for the literature relating cholinergic and anticholinergic drugs and avoidance responding. 24 references. (Author abstract modified)

001812 Monder, Harvey. State University of New York at Binghamton **Effects of prenatal amphetamine on the development of behavior in rats.** (Ph.D. dissertation). Dissertation Abstracts International. 39(10):5121-B, 1979. Ann Arbor, Univ. Microfilms No. 7908431, 85p., 1979.

The effects of prenatal amphetamine on the development of behavior in rats were investigated. Female rats were treated with either 0, 2, or 5mg/kg d-amphetamine sulfate mixed with their drinking water begun 30 days before they were mated. Drug treatment was discontinued at parturition. Results indicate that pregnant females treated with amphetamine have offspring that show a retardation in some physical indices of development. A behavioral effect of the drug on some behaviors that decreases with age was also found. These differences in development are taken to be more related to prenatal drug influences than postnatal maternal effects, as maternal/offspring observations did not indicate differences between the groups. (Journal abstract modified)

001813 Monder, Harvey; Yasukawa, Norie; Christian, John J. Dept. of Biological Sciences, State University of New York, Binghamton, NY 13901 **Perinatal naloxone: when does naloxone affect hyperalgesia?** *Pharmacology Biochemistry and Behavior*. 11(2):235-237, 1979.

Pregnant mice were treated with naloxone via subcutaneous implants from about 5 days prior to parturition. At birth, entire litters were cross-fostered so that groups of offspring were exposed to naloxone treated mothers before birth, after birth to weaning, from about 5 days before birth to weaning, or not exposed to naloxone. When tested on a hotplate at 50 days of age, females either prenatally treated or prenatally and postnatally treated showed hyperalgesia to heat. For male offspring, this effect was not evident. This sex difference may have been induced by the cross-fostering procedure. 21 references. (Author abstract)

001814 Mucha, R. F. Addiction Research Foundation, Toronto, Ontario M5S 2S1, Canada **Effect of naloxone and morphine on guinea pig tonic immobility.** *Behavioral and Neural Biology*. 28(1):111-115, 1980.

Tonic immobility produced by placing male adult guinea-pigs on their backs was dose dependently facilitated by ip morphine-SO4(0, 1.2, 6, and 30mg/kg), but not significantly affected by i.p. naloxone-HCl(0, 0.6, 3, and 15mg/kg). However, 2mg/kg naloxone (i.p.) significantly reduced the facilitation of tonic immobility produced by 30mg/kg morphine. The morphine effect is consistent with a role for endogenous opioid peptides in tonic immobility. The naloxone data, however, indicate that micro-opiate receptor involvement is unlikely. 12 references. (Author abstract)

001815 Mucha, R. F.; Kalant, H. Dept. of Pharmacology, University of Toronto, Toronto, Ontario, Canada M5S 2S1 **Increased weight gain as a morphine withdrawal response in rats.** *Pharmacology Biochemistry and Behavior*. 11(2):197-201, 1979.

Weight change effects of morphine were investigated in two rat strains. Adult male Wistar rats, injected daily with 20 or 200mg/kg morphine-SO4 for 35 days, suffered a dose dependent weight loss over the first 3 days of morphine withdrawal. However, during the next 28 days they gained weight more rapidly than controls, the gains being related to previous morphine dosage. Findings were replicated in Sprague-Dawley rats treated for 26 days with 60mg/kg morphine. Food restricted controls suffering weight losses equal to those of morphine treated animals or morphine withdrawn groups did not subsequently gain weight as rapidly as the latter groups. Therefore, the rapid postwithdrawal weight gain may be a true adaptive response to the weight suppressing effects of morphine. Comparison of the two morphine treated strains indicated possible strain differences for tolerance to morphine's weight reducing effect. 29 references. (Author abstract modified)

001816 Murphy, James M.; Nagy, Z. Michael. Institute for Psychiatric Research, Indiana University Medical Center, Indianapolis, IN 46223 **FLA-63 blocks food-deprivation-induced behavioral arousal in the mouse.** *Physiological Psychology*. 7(4):407-411, 1979.

The effects of FLA-63, a dopamine-beta-hydroxylase inhibitor, on food-deprivation-induced locomotor arousal were investigated in mice using a daily 2 hour shuttle cage test. In Experiment 1, deprived mice demonstrated enhanced locomotor activity compared to ad lib controls. The pattern of the activity over 15 min intervals showed that the locomotor arousal was partly due to an attenuation of the normal within session activity decrease characteristic of controls. This finding suggests some inhibition of habituation processes as a result of food deprivation. Experiment 2 indicated an important role for norepinephrine systems in the mediation of the starvation induced arousal, as pretreatment with FLA-63 blocked locomotor arousal in food deprived mice. 25 references. (Author abstract modified)

001817 Myslobodsky, Michael S.; Mansour, Rita. Psychobiology Research Unit, Department of Psychology, Tel-Aviv University, Ramat-Aviv, Israel **Hypersynchronisation and sedation produced by GABA-transaminase inhibitors and picrotoxin: does GABA participate in sleep control? Waking and Sleeping.** 3(3):245-254, 1979.

The effects of GABA-transaminase inhibitors and picrotoxin on rats were studied. Systemic administration of gamma-acetylenic GABA (100mg/kg) or gamma-vinyl GABA (1200mg/kg) produced a behavioral picture of somnolence accompanied by EEG hypersynchronization reminiscent of electrographic signs of petit-mal epilepsy. Similarly, a systemic administration of GABA antagonist, picrotoxin (3-4mg/kg), produced a short lasting period of sedation preceding the development of myoclonic jerks which was also accompanied by wave-spike discharges. The role of GABA in sleep control is discussed. Re-

sults suggest that hyperactivity of GABA-ergic system as well as its hypoactivity could mediate pathological somnolence associated with different forms of epilepsy. 54 references. (Author abstract modified)

001818 Nausieda, Paul A.; Koller, William C.; Weiner, William J.; Klawans, Harold L. Dept. of Neurological Sciences, Rush Presbyterian-St. Luke's Medical Center, 1725 West Harrison, Chicago, IL 60612 **Modification of postsynaptic dopaminergic sensitivity by female sex hormones.** *Life Sciences*. 25(6):521-526, 1979.

Stereotyped behavior in response to d-amphetamine or apomorphine was significantly reduced in female guinea-pigs following oophorectomy in a study of the effect of oophorectomy and subsequent estrogen and progesterone replacement. Responsiveness to either dopamine agonist was significantly increased by the subsequent chronic administration of either estradiol valerate or progesterone. Modification of postsynaptic dopaminergic sensitivity by female sex hormones may underlie the clinical association of hyperkinetic movement disorders, psychosis or depression seen with alterations in female sex hormones in man. 16 references. (Author abstract modified)

001819 Nemeroff, Charles B.; Prange, Arthur J., Jr. Dept. of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Neurotensin: perchance an endogenous neuroleptic? (Unpublished paper).** Research Report, NIMH Grant MH-32316, 1979. 31 p.

Certain properties of neurotensin (NT) were compared with neuroleptic agents. Like neuroleptics, NT injected intracisternally (i.c.) or intracerebroventricularly (but not peripherally) produces: 1) potentiation of barbiturate sedation, 2) hypothermia, 3) diminished locomotor activity, and 4) muscle relaxation. Treatments which reduce the functional activity of dopamine (DA) circuits (6-hydroxydopamine-induced DA depletion or haloperidol pretreatment) augment NT-induced hypothermia. In addition, bilateral nucleus accumbens injections of NT, like haloperidol, significantly antagonized increased locomotor activity and rearing induced by d-amphetamine. The hypothermia and muscle relaxation induced by both NT and neuroleptics is antagonized by i.c. injection of thyrotropin releasing hormone, the endogenous tripeptide. Unlike neuroleptic drugs, NT did not inhibit the binding of 3H-spiroperidol to the DA receptors in either the nucleus caudatus or the nucleus accumbens. NT was found to be a potent antinociceptive agent. It was more potent on a molar basis than met-enkephalin, leu-enkephalin, and morphine, but less potent than beta-endorphin. These findings, taken together, support the hypothesis that NT is a neuromodulator. It is a neuropeptide which shares many but not all properties with neuroleptic agents. 41 references. (Author abstract modified)

001820 Nistico, G.; Rotiroli, D.; De Sarro, A.; Naccari, F.; Stephenson, J. D. Institute of Pharmacology, Faculty of Medicine, University of Messina, Messina, Italy **Central effects of histamine and H1 and H2 receptor agonists and antagonists after intraventricular infusion in fowls.** *Research Communications in Chemical Pathology and Pharmacology*. 27(3):431-450, 1980.

Behavior, electrocortical activity, and body temperature were studied in adult fowls (*Gallus domesticus*) following infusion of histamine and related drugs into the third cerebral ventricle. Histamine produced an initial period of electrocortical synchronization followed by a longer lasting period of behavioral stimulation, electrocortical desynchronization, and shivering; body temperature was increased in a dose dependent manner. The H2-receptor agonist dimaprit produced behavioral and electrocortical sleep and decreased body temperature. The H1 receptor

agonist 2-(2-thiazolyl)-ethylamine produced behavioral stimulation, electrocortical desynchronization, vocalization, and hyperthermia. Cimetidine, an H₂-receptor antagonist, produced intense behavioral stimulation and electrocortical desynchronization accompanied by vocalization, tachypnoea, occasional escape responses, and stereotypies; body temperature was increased. Mepyrmine, and H₁-receptor antagonist, produced behavioral and electrocortical sleep and prevented the behavioral excitation and hyperthermia induced by histamine and the H₁-receptor agonist, respectively. Haloperidol failed to antagonize the histamine-induced behavioral excitation. 54 references. (Author abstract modified)

001821 Nozaki, Masako; Bell, James A.; Martin, William R. Dept. of Pharmacology, College of Medicine, University of Kentucky, Lexington, KY 40536 **Noradrenergic action of amphetamine following degeneration of descending monoaminergic fibers in the spinal cord.** *Psychopharmacology*. 67(1):25-29, 1980.

The noradrenergic action of amphetamine following degeneration of descending monoaminergic fibers in the spinal cord was investigated in rats. Amphetamine and methoxamine facilitated the flexor reflex in chronic spinal rats whose descending monoaminergic nerve endings were degenerated. Methoxamine, but not amphetamine, facilitated the flexor reflex in the chronic spinal rat 16 to 20 hours after i.v. 6-hydroxydopamine treatment. These data indicate that amphetamine's spinal cord facilitative effects are mediated through two noradrenergic mechanisms. In the acute spinal rat, amphetamine's facilitative actions require the integrity of the sympathetic nervous system. 35 references. (Author abstract modified)

001822 Oberlander, Claude; Euvrard, Catherine; Dumont, Claude; Boissier, Jacques R. Centre de Recherches Roussel-Uclaf, 111 route de Noisy, F-93230 Romainville, France **Circling behaviour induced by dopamine releasers and/or uptake inhibitors during degeneration of the nigrostriatal pathway.** *European Journal of Pharmacology*. 60(2/3):163-170, 1979.

Benzylpiperazine, d-methamphetamine, d-amphetamine, and l-amphetamine induced ipsilateral circling in male Sprague-Dawley rats 6 weeks after unilateral 6-hydroxydopamine lesions of the nigrostriatal dopamine (DA) pathway, but induced contralateral turning when tested 24 hours after the lesion. Methylphenidate, pipradrol, p-chloroamphetamine, mazindol, nomifensine, and benzotropine induced ipsilateral turning in animals with acute or chronic lesions. Additional studies were made in rats treated with pargyline, apomorphine, reserpine, or alpha-methyl-p-tyrosine. Results suggest that drugs that induce contralateral turning during the degeneration of the nigrostriatal pathway act by releasing newly synthesized DA independently of nerve impulse flow, while drugs that induce ipsilateral turning in acute lesion model inhibit uptake of DA or inhibit release of the reserpine sensitive DA pool. 31 references. (Author abstract modified)

001823 Oehme, Peter; Hilde, Heinz; Morgenstern, Eveline; Gores, Erhard. Institute for Drug Research, Academy of Sciences of the G.D.R., DDR-1136 Berlin, Germany **Substance P: does it produce analgesia or hyperalgesia?** *Science*. 208(4441):305-307, 1980.

The capability of substance P (SP) to produce analgesia or hyperalgesia was studied in mice. In the hot plate test, SP given intravenously caused analgesia at doses of 0.00005 and 0.0005 gram per kilogram, while lower doses caused hyperalgesia. The influence of SP on nociception depended on the individual mouse's sensitivity to pain (control response latency). Analgesia was produced by SP administered to mice with high sensitivity to thermic stimulation, whereas hyperalgesia occurred in mice

whose control latencies were longer than normal. This result is interpreted as an indication that SP is capable of normalizing responsiveness to pain and could be classified as a regulatory peptide. 7 references. (Author abstract modified)

001824 Orikasa, Syuzo; Sakurada, Shinobu; Kisara, Kensuke. Kisara: Dept. of Chemical Pharmacology, Tohoku College of Pharmacy, Komatsushima, Sendai 983, Japan **Head-twitch response induced by tyramine.** *Psychopharmacology*. 67(1):53-59, 1980.

The relationship between serotonergic and catecholaminergic systems in the head twitch response induced by tyramine (TyA) was investigated. The intracerebroventricular (IC) administration of TyA induced a characteristic head twitch response in mice pretreated with safrazine, a monoamine oxidase (MAO) inhibitor. Safrazine pretreated mice exhibited similar head twitches following the IC treatment of serotonin (5-HT). The maximum dose of 5-HT which did not elicit head twitches significantly potentiated TyA-induced head twitches. Antiserotonergic drugs such as morphine dimethothiazine antagonized TyA-induced head twitches. A serotonergic denervator, 5,6-dihydroxytryptamine, potentiated head twitch induced by TyA or 5-HT. Both TyA-induced and 5-HT-induced head twitches were inhibited by dopamine and noradrenaline, while catecholaminergic denervators such as reserpine and 6-hydroxydopamine, and diethyldithiocarbamic acid, a dopamine-beta-hydroxylase inhibitor, increased the TyA response. These results indicate that head twitches induced by TyA may be mediated via the serotonergic system and may inhibit the catecholaminergic system. 36 references. (Author abstract modified)

001825 Ossenkopp, Klaus-Peter. York University (Canada) **The partial reinforcement effect and the motivational properties of frustration: investigating the effects of amobarbital on primary and secondary frustration.** (Ph.D. dissertation). Dissertation Abstracts International. 39(11):5616-B, 1979. (Not available from Univ. Microfilms), 1978.

A series of four food rewarded runway experiments examined the effects of reward magnitude and administration of sodium amobarbital on the extinction partial reinforcement effect (PRE) and the frustration effect (FE) in rats. In general, a positive relationship was observed between reward size and magnitude of the FE, and between reward size and magnitude of the PRE following extended acquisition training. Injections of amobarbital failed to reduce the magnitude of the FE and the aversiveness of the empty foodcup on nonreinforced trials. The drug eliminated the PRE following extended acquisition but failed to reduce the magnitude of the PRE following limited acquisition. The data are consistent with Amsel's frustration theory and with Brooks' nonconditioning interpretation of the small trials PRE. (Journal abstract modified)

001826 Owen, F.; Cross, A. J.; Waddington, J. L.; Poulter, M.; Gamble, S. J.; Crow, T. J. Division of Psychiatry, MRC Clinical Research Centre, Harrow, Middlesex, HA1 3UJ, England **Dopamine-mediated behaviour and 3H-spiroperone binding to striatal membranes in rats after nine months haloperidol administration.** *Life Sciences*. 26(1):55-59, 1980.

Rats were treated with haloperidol (1.5mg/kg/day) in their drinking water for 9 months, with or without a subsequent withdrawal period of 7 to 10 days. Compared with controls, spontaneous locomotion and apomorphine-induced stereotypy were reduced in rats maintained on haloperidol whereas both behaviors were increased after the withdrawal period. Maximum specific 3H-spiroperone binding to striatal membrane preparations was increased about 65% in drug treated rats with or without a withdrawal period. The dissociation constant for 3H-spiroperone bind-

ing was significantly increased only in those rats maintained on haloperidol with no withdrawal period. The increase in maximum binding of 3H-spiperone was larger than that reported after less prolonged administration of neuroleptics. It is suggested that the size of the change should be taken into account in assessing the increased ligand binding reported in postmortem brains of schizophrenics. 11 references. (Author abstract)

001827 Palfai, Tibor; Walsh, Thomas J. Psychology Research Laboratory, Syracuse University, Syracuse, NY 13210 **The role of peripheral catecholamines in reserpine-induced amnesia.** *Behavioral and Neural Biology.* 27(4):423-432, 1979.

The effect of peripherally administered catecholamines on reserpine-induced amnesia of passive-avoidance training in mice was investigated. The amnesic effect of reserpine could be blocked with 50mg/kg dopamine (DA) or 0.1 or 0.75mg/kg norepinephrine when given before, immediately, or 10 min after but not 90 min following passive-avoidance. Epinephrine or a lower dose of DA could not attenuate the reserpine-induced amnesia. Syrosingopine, the peripherally acting reserpine analogue, also produced time dependent retention impairments. The amnesic effects of these Rauwolfia alkaloids are interpreted in terms of their peripheral antiadrenergic actions. 42 references. (Author abstract)

001828 Panksepp, Jaak; Najam, Najma; Soares, Frieda. Dept. of Psychology, Bowling Green State University, Bowling Green, OH 43403 **Morphine reduces social cohesion in rats.** *Pharmacology Biochemistry and Behavior.* 11(2):131-134, 1979.

The effect of low (1mg/kg) doses of morphine on maintenance of physical proximity was evaluated in paired rats observed in a four foot square test area. Morphine reliably reduced proximity maintenance time, and this was apparently not due to sedation, since the effect was unmodified by doses of amphetamine which substantially increased motor activity. The effects of naloxone were inconsistent with this measure of social motivation. In general, the results are consistent with the theoretical proposition that a brain neurochemical change which might lead to social attraction is the activation of endogenous opioid systems. When opiate activity is exogenously sustained, animals exhibit a subnormal tendency to be gregarious. 19 references. (Author abstract)

001829 Papadopoulos, Georges; Huston, Joseph P. Houston: Institute of Psychology, University of Dusseldorf, Universitätsstrasse 1, D-4000 Dusseldorf, Germany **Removal of the telencephalon spares turning induced by injection of GABA agonists and antagonists into the substantia nigra.** *Behavioural Brain Research.* 1(1):25-38, 1980.

The effects of removal of the telencephalon on the turning behavior induced by injection of GABA agonists and antagonists into the substantia nigra were investigated. Unilateral injections into the substantia nigra of GABA agonists or the GABA-related agents muscimol, baclofen, or beta-aminobutyric acid induced intensive turning in the direction contralateral to the injected hemisphere. Intraneural injection of the GABA antagonist picrotoxin led to ipsiversive turning. Surgical removal of the whole telencephalon (including the neocortex, hippocampus, striatum, septal nuclei, and amygdalae) influenced neither direction nor magnitude of the turning responses induced by these various drugs. A GABAergic system in the substantia nigra can, therefore, cause turning independent of telencephalic structures. 43 references. (Author abstract modified)

001830 Persson, Sven-Ake. Dept. of Pharmacology, University of Umea, S-901 87 Umea, Sweden **The effects of chlorimipramine and protriptyline on tube running activity in mice.** *Pharmacology Biochemistry and Behavior.* 12(2):255-258, 1980.

The effects of drugs on specific behavior in mice was studied using the new technique of tube running activity. The time it takes for a mouse to run 100 cm in a narrow tube is measured. During the first 2 hours after the administration of chlorimipramine (7.5mg/kg i.p.) there was a decreased run time as compared with controls. The run time could not be further decreased by increasing the dose of chlorimipramine, but the effect was prolonged. Protriptyline in the dose range of 3.75 through 30mg/kg had no observable effect on the run time, but protriptyline 60mg/kg decreased the run time in the same way as chlorimipramine 60mg/kg did. The decreased run time after protriptyline 60mg/kg is probably due to a blockage of the amine pump in the 5-hydroxytryptamine neurons at this high dose. These results suggest that tube running activity more specifically measures functional effect of 5-hydroxytryptamine than functional effects of noradrenaline. 17 references. (Author abstract modified)

001831 Persson, Sven-Ake; Wahlstrom, Goran. Dept. of Pharmacology, University of Umea, S-901 87 Umea, Sweden **Tube running activity in mice: a method to evaluate the behavioural effects of drugs.** *Pharmacology Biochemistry and Behavior.* 12(2):259-264, 1980.

The effects of various environmental factors were measured using the new technique of tube running activity in mice. The time it takes for a mouse to run 100 cm is measured. The most important factor was found to be the frequency of testing. With repeated testing the run time was increased, which probably is due to a decrease in exploratory activity. However, tube running seems not to be a specific measure of exploratory activity. Administration of nialamide alone, as well as combined with 5-hydroxy-DL-tryptophan, gave a dose dependent decrease in run time. The results suggest that tube running activity may be useful for measuring 5-hydroxy-tryptamine mediated behavior. 13 references. (Author abstract modified)

001832 Pirch, J. H. Dept. of Pharmacology and Therapeutics, Texas Tech University School of Medicine, Lubbock, TX 79430 **Effects of dextroamphetamine on event-related slow potentials in rat cortex during a reaction time task.** *Neuropharmacology.* 19(4):365-370, 1980.

The effects of dextroamphetamine on event related slow potentials recorded from two different cortical areas in the rat during an operant reaction time task in which trials were initiated at variable intervals by an auditory warning stimulus were investigated. Slow potential responses during the 2 second period between onset of the warning stimulus and extension of a retractable lever were analyzed as a function of various doses of dextroamphetamine. Surface negative slow potential responses from the frontal cortex had two components, an early wave which reached maximum amplitude at 200 to 350msec after the stimulus and a later wave which began at 650 to 850 msec. The slow potential response recorded from the visual cortex showed a smaller surface negative wave which was maximum at 350 to 1000 msec; following the initial negative wave, the potential gradually shifted positive. Dextroamphetamine caused a dose related depression of the frontal slow potential responses (indicated by both amplitude and area analysis). Amplitudes and areas of the visual slow potential were not consistently altered. Results of the study indicate that the effect of d-amphetamine on event related slow potentials in the rat are dependent on the cortical area from which they are recorded. 35 references. (Author abstract modified)

001833 Polc, P.; Schneeberger, J.; Haefely, W. Pharma Research Department, Building 69/70, F. Hoffmann-La Roche & Co. Ltd., Grenzacherstrasse 124, CH-4002 Basle, Switzerland

Effects of several centrally active drugs on the sleep-wakefulness cycle of cats. *Neuropharmacology*. 18(3):259-267, 1979.

The effects of 18 psychotropic drugs, including several antidepressants, on the sleep/wakefulness cycle were studied in cats, using telemetric EEG and electromyographic recording. At the lowest i.p. dose that affected the sleep/wakefulness cycle, the antidepressants imipramine, clomipramine, desipramine, amitriptyline, nortriptyline, maprotilene, Ro03-5939, mianserin, iprindole, viloxazine, pargyline, and Ro11-1163 selectively depressed REM sleep, as did 5-hydroxy-L-tryptophan. Other psychotropic drugs reduced REM sleep but simultaneously affected NREM sleep at minimum effective doses: lysergic acid diethylamide and methylphenidate depressed NREM sleep, and cyproheptadine augmented NREM sleep. Chlorpromazine and haloperidol had only weak effects on sleep parameters. Results indicate that antidepressant drugs exert a selective suppressant effect on REM sleep, which may reflect increased activation of 5-hydroxytryptamine or noradrenaline receptors in brain. 49 references. (Author abstract modified)

001834 Porrino, Linda J.; Coons, Edgar E. Coons: Dept. of Psychology, New York University, 6 Washington Place, New York, NY 10003 **Effects of GABA receptor blockade on stimulation-induced feeding and self-stimulation.** *Pharmacology Biochemistry and Behavior*. 12(1):125-130, 1980.

The effects of GABA receptor blockade on stimulation-induced feeding and self-stimulation were investigated. Frequency thresholds for eating elicited by electrical stimulation of the lateral hypothalamus of rats decreased in a dose dependent manner after i.p. administration of picrotoxin, a GABA antagonist that blocks GABA mediated synaptic inhibition. Strychnine (i.p.), a glycine antagonist that blocks glycine mediated synaptic inhibition, had no effect. By contrast, frequency thresholds for self-stimulation at the same electrode site significantly increased after picrotoxin. Again, strychnine had no effect. These findings indicate that GABAergic mechanisms are involved in both electrically elicited feeding and self-stimulation. They also suggest a dissociation of the neural substrates which subserve these behaviors. 34 references. (Author abstract modified)

001835 Post, Robert M.; Jimerson, David C.; Bunney, William E., Jr.; Goodwin, Frederick K. NIH, 9000 Rockville Pike, Building 10, Room 3S239, Bethesda, MD 20205 **Dopamine and mania: behavioral and biochemical effects of the dopamine receptor blocker pimozide.** *Psychopharmacology*. 67(3):297-305, 1980.

Behavioral and biochemical effects of the dopamine receptor blocker pimozide were investigated in manic patients. It is reported that in manic patients pimozide produces substantial clinical improvement with a magnitude and time course similar to that observed with the more routinely used phenothiazines chlorpromazine and thioridazine. Pimozide did not significantly increase probenecid-induced accumulations of the dopamine metabolite homovanillic acid (HVA) compared to pretreatment values. Higher HVA values were observed in manic than in nonmanic patients, however. These clinical and biochemical data add to a growing body of indirect evidence that a dopaminergic alteration may be associated with some components of the manic syndrome. 88 references. (Author abstract modified)

001836 Prado-Alcala, Roberto A.; Kaufmann, Patricia; Moscona, Renee. Physiology Dept., School of Medicine, National University of Mexico, P. O. Box 70250, Mexico 20, D.F., Mexico **Scopolamine and KCl injections into the caudate nucleus. Overtraining-induced protection against deficits of learning.** *Pharmacology Biochemistry and Behavior*. 12(2):249-253, 1980.

To test the hypothesis that extended training of an instrumental task prevents the performance impairments seen after cholin-

ergic and generalized blockade of caudate putamen complex (NC) activity in animals with a relatively low degree of training, groups of rats were trained to press a lever under a continuous reinforcement schedule for 5, 15, or 20 sessions. The effects of microinjections of scopolamine and potassium chloride into the CN were then assessed. In agreement with early studies in cats, a significant deficit in performance was produced in the animals with a low or medium degree of training, while no changes in learned behavior were seen in the overtrained rats. These results show that: normal neural activity of the CN is essential for performance of instrumental behavior during acquisition and early maintenance stages but not after overtraining, and that after extended training the encoding necessary for performance may be transferred to another neural system outside the CN. 14 references. (Author abstract)

001837 Pray, Sidney Lucius, Jr. Texas Christian University **The effects of epinephrine and norepinephrine on emotional behavior in rats and Siamese fighting fish.** (Ph.D. dissertation). Dissertation Abstracts International. 39(9):4641-B, 1979. Ann Arbor, Univ. Microfilms No. 7906065, 74p., 1967.

The effects of epinephrine and norepinephrine on shock-induced reflexive fighting behavior in rats and in female Siamese fighting fish were examined. The effects of differential levels of norepinephrine on conditioned suppression of the consummatory drinking response in rats were also assessed. Norepinephrine significantly increased the frequency of reflexive fighting in rats but the hypothesis that injected epinephrine would decrease this rate was not supported. Norepinephrine potentiated the agonistic response in female Siamese fighting fish as was indicated by measures based on total duration of agonistic display to a mirror image. However, latency and frequency measures failed to support the hypothesis. It is indicated that central norepinephrine is involved as a mediator in aggression as well as fear and perhaps in emotional behavior generally. (Journal abstract modified)

001838 Racine, Ronald; Burnham, W. M.; Livingston, Kenneth. Department of Psychology, McMaster University, Hamilton, Ontario, Canada **The effect of procaine hydrochloride and diazepam, separately or in combination, on cortico-generalized kindled seizures.** *Electroencephalography and Clinical Neurophysiology*. 47(2):204-212, 1979.

The effects on cortically kindled seizure responses of procaine hydrochloride, diazepam, and combinations of these two drugs were tested. The cortex was stimulated until seizure responses developed past the focal stage to the cortico generalized stage. Diazepam was found to block the generalized component of the cortico generalized electrographic and motor seizure leaving the tonic only slightly suppressed. Procaine blocked the tonic leaving the clonic seizure and discharge that is characteristic of the generalized response relatively intact. Combinations of half doses of the two drugs are reported to completely block all electrographic and motor seizure responses in about half the animals. 14 references. (Author abstract modified)

001839 Rainbow, Thomas C.; Hoffman, Paula L.; Flexner, Louis B. Dept. of Anatomy, University of Pennsylvania School of Medicine, Philadelphia, PA 19104 **Studies of memory: a re-evaluation in mice of the effects of inhibitors on the rate of synthesis of cerebral proteins as related to amnesia.** *Pharmacology Biochemistry and Behavior*. 12(1):79-84, 1980.

The hypotheses that the degree of inhibition of cerebral protein synthesis either at training or following training is the critical variable that determines the degree of amnesia were tested. As a first step it was found that the concentrations of numerous cerebral amino acids were substantially increased in two strains of mice 30 minutes after treatment with amnesic doses of the in-

hibitors of protein synthesis, cycloheximide (CXM) and anisomycin. This observation led, in several different experiments, to a comparison of the apparent degree of inhibition of protein synthesis derived from the acid soluble radioactivity with that derived from the specific radioactivity of tyrosine tagged with L(1-14C)-tyrosine. In all instances, the apparent degree of inhibition was decreased when based upon tyrosine's specific radioactivity. The effect of several treatments with CXM on memory of a trial passive-avoidance task provided data for analysis of the relationship between the degrees of amnesia and those of the more accurate estimates of inhibition of protein synthesis based upon the specific radioactivity of tyrosine. Results failed to support the views that the level of inhibition of protein synthesis at or after training are entirely sufficient to account for the behavioral results. The results also suggest that CXM produces with time some direct or indirect change in the brain that antagonizes the amnesic effects of the antibiotic and that consequently contributes to the survival of memory in mice trained 2 hours after a large amnesic dose of CXM. 29 references. (Author abstract modified)

001840 Raleigh, M. J.; Brammer, G. L.; Yuwiler, A.; Flannery, J. W.; McGuire, M. T.; Geller, E. Neurobiochemistry Laboratory T-85, Veterans Administration Medical Center, Los Angeles, CA 90073 Serotonergic influences on the social behavior of vervet monkeys (*Cercopithecus aethiops sabaeus*). *Experimental Neurology*. 68(2):322-334, 1980.

The behavioral effects of altering serotonin neurotransmission by chronic drug treatments in socially living vervet monkeys (*Cercopithecus aethiops sabaeus*) were examined. Animals received tryptophan (TRP, 20mg/kg/day), parachlorophenylalanine (PCPA, 80mg/kg/day), 5-hydroxytryptophan (5-HTP, 40mg/kg/day), chlorglyline (10mg/kg/day), or PCPA followed by concurrent PCPA and 5-HTP. Grooming, approaching, resting, and eating were increased by TRP and decreased by PCPA; TRP decreased and PCPA increased locomoting, avoiding, being solitary, and being vigilant. Grooming, being vigilant, and receiving aggression were increased by 5-HTP, and PCPA increased initiating aggression and decreased huddling. Concurrent administration of 5-HTP and PCPA reversed the effects of PCPA on approaching, grooming, and resting; augmented the PCPA effects on avoiding, being solitary, and aggression; and did not alter the PCPA effects on eating, locomoting, and huddling. Chlorglyline increased grooming, approaching, and being vigilant and decreased being solitary. No treatment significantly affected sexual behavior. These data suggest that serotonergic systems contribute relatively substantially to the mediation of grooming and approaching, participate less strongly in resting and locomoting, are implicated still more weakly in being solitary, avoiding, and being vigilant, and have little if any involvement in huddling, aggression, and sexual behavior. 39 references. (Author abstract)

001841 Reinisch, June Machover; Simon, Neal G.; Gandelman, Ronald. Dept. of Psychology, Busch Campus, Rutgers University, New Brunswick, NJ 08903 Prenatal exposure to prednisone permanently alters fighting behavior of female mice. *Pharmacology Biochemistry and Behavior*. 12(2):213-216, 1980.

Female mice born of mothers administered 100mcg of prednisone on days 13 through 18 of gestation were studied. These mice attacked a stimulus male significantly sooner following the commencement of testosterone treatment in adult life than did mice born of control mothers. In a sec. experiment, significantly fewer prenatally prednisone exposed females displayed postpartum aggression as compared to controls. In both experiments females of the 100mcg prednisone group showed a reduction in birth weight relative to controls. The effect on body weight did not persist since no differences were observed on day 21 of life.

The data show that prenatal exposure to prednisone permanently modifies the later intraspecific fighting behavior of female mice. 20 references. (Author abstract)

001842 Revusky, Sam; Taukulis, Harald K.; Peddle, Calvin. Memorial University of Newfoundland, St. John's, Newfoundland, A1C 5S7, Canada Learned associations between drug states: attempted analysis in Pavlovian terms. *Physiological Psychology*. 7(4):352-363, 1979.

The avail (aversion failure) effect in rats was analyzed in Pavlovian terms. A sedative dose of pentobarbital was injected into rats 30 min. prior to a toxic dose of lithium on a number of occasions. A later test indicated that pentobarbital had lost its normal capacity to produce a mild aversion to previously consumed saccharin solutions as a result of these pairings. This avail effect is opposite to predictions based upon principles of Pavlovian higher order conditioning. Attempts to implicate conditioned inhibition in avail were unsuccessful, but led to discovery of another effect, called conditioned sickness, which also resulted from pairing of pentobarbital with lithium. While rats were sedated with pentobarbital, they avoided drinking novel saccharin solution. Conditioned sickness looked like straightforward Pavlovian conditioning until it was found not to be obtainable when other mild drugs were substituted for pentobarbital. Thus neither avail nor conditioned sickness was congruent with traditional Pavlovian principles of conditioning. Nevertheless, the avail effect seems to involve learning because of its occurrence when a variety of drugs are substituted for pentobarbital or for lithium. Apparently, then, the learning involving association of feeling states, which probably has an important role in homeostasis, follows laws which are now undiscovered. 21 references. (Author abstract modified)

001843 Ridley, R. M.; Baker, H. F.; Scraggs, P. R. Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow, England The time course of the behavioral effects of amphetamine and their reversal by haloperidol in a primate species. *Biological Psychiatry*. 14(5):753-765, 1979.

A group of six marmosets was administered amphetamine (Phase 1), amphetamine plus haloperidol (Phase 2), and then amphetamine alone (Phase 3) over consecutive periods of 27, 51, and 33 days after which drug treatment was terminated (Phase 4). Five mutually exclusive categories of behavior were assessed during the experiment: social contact, inactivity, self-grooming habits, rapid head movements, and locomotion. The time course of the effects of amphetamine and haloperidol on the different behavioral categories suggests that different mechanisms may be involved in each case. The time course of haloperidol is seen as resembling the time course of the antipsychotic effect of neuroleptics in man. It is reported that some effects of amphetamine are not reversed by haloperidol, and some effects of withdrawal of haloperidol do not have an obvious counterpart in the clinical situation. 28 references. (Author abstract modified)

001844 Ridley, R. M.; Baker, H. F.; Weight, M. L. Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow, HA1 3UJ, England Amphetamine disrupts successive but not simultaneous visual discrimination in the monkey. *Psychopharmacology*. 67(3):241-244, 1980.

The effects of amphetamine on successive and simultaneous visual discrimination in the monkey was investigated. Three adolescent marmosets were trained on simultaneous and successive versions of a red/white visual discrimination task. The effects of doses of 0.2 and 1.2mg/kg D-amphetamine on the performance of these tasks were assessed using a balanced design. It was found that while there was no drug effect on performance of the simultaneous task, amphetamine exerted a dose de-

pendent disruptive effect on the successive version of the task. It is argued that amphetamine disrupts response control rather than discriminative ability and, in this respect, resembles the effect of orbitofrontal and limbic lesions in contrast to other neocortical lesions. 18 references. (Author abstract modified)

001845 Ridley, R. M.; Scraggs, P. R.; Baker, H. F. Division of Psychiatry, Clinical Research Center, Harrow, England **The effects of metoclopramide, sulpiride, and the stereoisomers of baclofen on amphetamine-induced behavior in the marmoset.** *Biological Psychiatry*. 15(2):265-274, 1980.

The effects on amphetamine-induced behavior in six marmosets of drugs sometimes used in the treatment of psychosis were studied. Marmosets were treated with either saline or amphetamine followed after 18 minutes by doses of either metoclopramide, sulpiride, or the D-isomers or L-isomers of baclofen. Metoclopramide antagonized amphetamine-induced behavior at low doses while also causing sedation at higher doses in control animals. Neither sulpiride nor baclofen specifically antagonized amphetamine-induced behavior. 27 references. (Author abstract modified)

001846 Rigter, H.; Hannan, T. J.; Messing, R. B.; Martinez, J. L., Jr.; Vasquez, B. J.; Jensen, R. A.; Veliuette, J.; McGaugh, J. L. CNS Pharmacology Dept., Scientific Development Group, Organon, Oss, The Netherlands **Enkephalins interfere with acquisition of an active avoidance response.** *Life Sciences*. 26(5):337-345, 1980.

The application of Leu-enkephalin and Met-enkephalin at a dose of 400mcg/kg, i.p. significantly impaired rats' acquisition of a one way active avoidance response. D-Ala-D-Leu-enkephalin also impaired acquisition but at a lower dose. D-Ala-Met-enkephalinamide in a wide dose range did not alter acquisition of the response. A high dose of naloxone blocked the impairing action of Leu-enkephalin. Results are discussed in terms of multiple opiate receptor species. 19 references. (Author abstract)

001847 Roberge, Andree G.; Boisvert, Claire; Everett, James. Dept. de Biochimie, Faculté de Médecine, Université Laval, Québec, Canada G1K 7P4 **Monoamine roles in retention and reversal of delayed response in cats.** *Pharmacology Biochemistry and Behavior*. 12(2):229-234, 1980.

The effect of manipulation of central monoamines upon behavior in a delayed response (DR) situation was studied in two experiments. In the first study, serotonin (5-HT) levels were increased by administration of 5-hydroxy-L-tryptophan (5-HTP) and R04-4602, a decarboxylase inhibitor, to cats who had overlearned the DR. This intervention had no significant effect upon performance in the sec. delay condition, but significantly increased error and nonresponse scores during delay trials; the effect is specific to an information holding demand upon the animal and according to the neurochemical analysis appears to be due to a central effect of 5-HT. In a sec. experiment, dopamine levels were raised by L-DOPA administration during a reversal of the original DR situation, and the effect of L-DOPA on the evolution of response strategies was observed. All animals developed a position habit that proved impossible to correct but L-DOPA animals developed a significant position habit more quickly than controls, thus suggesting a possible relationship between the neostriatal dopamine accumulation and behavioral plasticity. 27 references. (Author abstract)

001848 Rondouin, Gerard; Baldy-Moulinier, Michel; Passouant, Pierre. Laboratoire de Pathologie Experimentale, Institut de Biologie, Bd. Henri IV, F-34000 Montpellier, France **The influence of hippocampal kindling on sleep organization in cats. Effects of alpha-methylparatyrosine.** *Brain Research*. 181(2):413-424, 1980.

The effects of daily electrical stimulation of the ventral hippocampus on the sleep/waking cycle were studied in cats. Paradoxical sleep (PS) decreased as kindling progressed over a 61 day period, but waking and slow wave sleep (SWS) were not significantly altered. Intercatal discharges were facilitated by SWS and inhibited by PS and waking. Treatment with alpha-methylparatyrosine increased PS, but delayed kindling in some animals. 28 references. (Author abstract modified)

001849 Rose, D. Dept. of Anatomy, University of Bristol, Medical School, University Walk, Bristol BS8 1TD, England **Facilitation of bicuculline- and picrotoxin-induced seizures by sodium valproate in rats.** *Archives Internationales de Pharmacodynamie et de Therapie*. 239(1):78-85, 1979.

The effects of sodium valproate (50 to 1200mg/kg i.p.) on the EEG seizure activity induced by bicuculline and picrotoxin in paralyzed, anesthetized male hooded Brattleboro rats were examined. Doses of valproate larger than 200mg/kg significantly increased seizures induced by either convulsant. The mechanism by which sodium valproate facilitates seizures induced by GABA antagonists is discussed. 34 references. (Author abstract modified)

001850 Rosecrans, J. A.; Glennon, R. A. Dept. of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Drug-induced cues in studying mechanisms of drug action.** *Neuropharmacology*. 18(12):981-989, 1979.

The use of drug cues to study the mechanism of action of psychoactive drugs is described. Drug cues can be characterized by attempting to substitute other psychoactive agents and by attempting to antagonize the cue with various receptor antagonists. The site of action of the cue can be identified by comparing the peripherally generated cue with the effects of the drug when injected directly into various brain sites, by attempting to mimic the peripherally generated cue by stimulating various CNS sites electrically, and by attempting to alter the cue through selective neurotoxic lesions of various brain sites. 28 references. (Author abstract modified)

001851 Rosenfeld, J. Peter; Rice, Peter E. Cresap Neuroscience Laboratory, Dept. of Psychology, Northwestern University, Evanston-Chicago, IL 60201 **Effects of naloxone on aversive trigeminal and thalamic stimulation, and on peripheral nociception: a hypothesis of selective action and variability in naloxone testing.** *Brain Research*. 178(2-3):609-612, 1979.

The effects of naloxone on reactions to peripheral nociceptive stimuli and aversive brain stimulation were examined in albino rats in the evening, when pain threshold is highest. Naloxone (20mg/kg i.p.) had no significant effect on any of the peripheral indices (latency to face rub following noxious facial heat, pawlick on the hotplate, and tailflick latency). However, naloxone produced significant hyperalgesia to stimulation of the trigeminal complex at 20 or 200Hz, but not stimulation of the ventrobasal complex. Results suggest that naloxone interferes with endogenous opiate action in a system descending to a primary to secondary afferent synaptic area in the trigeminal complex but does not block all opiate receptors on these neurons. 20 references.

001852 Rothenberg, S.; Schottenfeld, S.; Selkoe, D.; Gross, K. Alcohol and Drug Abuse Research Center, McLean Hospital, Belmont, MA 02178 **Specific oculomotor deficit after acute methadone. II. Smooth pursuit eye movements.** *Psychopharmacology*. 67(3):229-234, 1980.

Changes in smooth pursuit eye tracking of targets moving sinusoidally in horizontal and vertical planes before and after up to

10mg oral methadone were measured electrooculographically in nontolerant nondependent humans. Methadone depressed the gain of horizontal tracking movements at most frequencies tested (0.2 to 1.6Hz) without changing target eye phase relationships. Lack of change in target eye cross-correlation functions after methadone and examination of individual records indicate that gain reduction was due to the eye failing to follow the target to the full extent of target excursion (plus or minus five degrees from eyes straight ahead view). Possible mechanisms and the practical consequences of methadone action on smooth pursuit are discussed. 16 references. (Author abstract)

001853 Rymer, W. Z.; Hasan, Z. Dept. of Physiology and Neurology, Ward 5-319, Northwestern University Medical School, 303 E. Chicago Avenue, Chicago, IL 60611 **Absence of force-feedback regulation in soleus muscle of the decerebrate cat.** *Brain Research.* 184(1):203-209, 1980.

The magnitude of force feedback effects on soleus stretch reflexes in the decerebrate cat was examined using a pharmacologically mediated reduction in muscle contractility to create an reasoned that a dantrolene induced decline in muscle contractility should be compensated by an increased electromyogram (EMG) output. Although dantrolene produced a major reduction in stretch reflex stiffness, there was no discernible compensatory increase in EMG. It is suggested that there was no effective force feedback pathway in operation. 10 references.

001854 Samanin, R.; Mennini, T.; Ferraris, A.; Bendotti, C.; Borsini, F.; Garattini, S. Istituto di Ricerche Farmacologiche Eritrea, 62, I-20157 Milan, Italy **m-Chlorophenylpiperazine: a central serotonin agonist causing powerful anorexia in rats.** *Naunyn-Schmiedeberg's Archives of Pharmacology.* 308(2):159-163, 1979.

The effects of meta-chlorophenylpiperazine (mCPP) on catecholamine uptake and release and its anorectic activity were studied in the rat. mCPP inhibited serotonin (5-HT) and norepinephrine (NA) uptake by synaptosomes to the same extent. Dopamine (DA) uptake was less affected, and mCPP did not significantly increase monoamine release in synaptosomal preparations. mCPP produced a dose dependent reduction of food intake. This effect was prevented by pretreatment with methergoline, a serotonin antagonist. The effect was not modified by intraventricular injection of 6-hydroxydopamine, lesions of nucleus medianus raphe, or ventral noradrenergic bundle, or by pretreatment with penfluridol, propranolol, or phentolamine. Data suggest that mCPP induced decrease in food intake depends on its ability to act as a 5-HT agonist in the brain. The specificity of the effects on 5-HT suggests that mCPP could prove useful in studies aimed at elucidating the functional role of 5-HT in the CNS. 25 references. (Author abstract modified)

001855 Sandman, Curt A.; McGivern, Robert F.; Berka, Chris; Walker, J. Michael; Coy, David H.; Kastin, Abba J. Fairview Hospital, 2501 Harbor Blvd., Costa Mesa, CA 92626 **Neonatal administration of beta-endorphin produces** *Life Sciences.* 25(20):1755-1760, 1979.

Male and female rat pups were injected with beta-endorphin, naloxone, or a saline solution during postnatal days 2 to 7 and then tested for analgesia with the tail flick test at 90 days of age. Rats treated with beta-endorphin neonatally showed a significant elevation in threshold for painful thermal stimuli. Neonatal treatment with naloxone also elevated the threshold for thermal stimuli. Administration of naloxone to these rats as adults did not reverse the analgesic effects. It is concluded that early exposure to beta-endorphin results in permanent change in behavior, perhaps by altering the interaction of endogenous opiates with

their binding sites during a critical period of opiate receptor development. 23 references. (Author abstract modified)

001856 Sands, Stephen F.; Wright, Anthony A. Graduate School of Biomedical Sciences, University of Texas Health Science Center, Houston, TX 77025 **Enhancement and disruption of retention performance by ACTH in a choice task.** *Behavioral and Neural Biology.* 27(4):413-422, 1979.

The effect of adrenocorticotrophic hormone (ACTH) on enhancement and disruption of retention performance in a choice task was investigated with 120 male rats who escaped/avoided electric shock by moving into the lighted arm of a Y-maze. Posttrial ACTH injections at one dose (1 IU/kg) enhanced retention, and at another dose (1000 IU/kg) disrupted retention; the overall dose response function was an inverted U for the retention test conducted 24 hr after the original learning. Thus, ACTH was shown to affect retention performance of normal rats in a choice task. Delayed posttrial ACTH injections showed no enhancement or disrupted retention from which it is concluded that ACTH acts upon some residual (memory?) from the learning experience. 48 references. (Author abstract modified)

001857 Sanger, D. J. Dept. of Psychology, University College, PO Box 78, Cardiff, CFI 1XL, Wales **The effects of fenfluramine on schedule-induced drinking in rats.** *Pharmacology Biochemistry and Behavior.* 11(2):151-153, 1979.

The effects of fenfluramine (0.5, 1, 2, 4, 8mg/kg) and d-amphetamine (0.25, 0.5, 1, 2mg/kg) on schedule-induced (fixed interval 60 sec food reinforcement) drinking was examined in the rat. Both drugs produced dose related decreases in drinking, with d-amphetamine being approximately four times more potent than fenfluramine. D-amphetamine produced large increases in overall rates of lever-pressing and greatly decreased the duration of postreinforcement pauses. Fenfluramine exerted similar actions, but at all doses studied, these effects were much less than the effects of d-amphetamine. 19 references. (Author abstract modified)

001858 Satinder, K. Paul. Dept. of Psychology, Lakehead University, Thunder Bay, Ontario, Canada P7B 5E1 **Interaction among scopolamine, conditioned stimulus modality, genotype, and either-way avoidance behavior of rats.** *Psychopharmacology.* 67(1):97-99, 1980.

The effects of scopolamine were investigated on either way avoidance in three genetic lines of rats under auditory and visual conditioned stimuli (CS). In the either way task, the animal had the option to respond in either of the two directions available. In the genetic line selected for high avoidance, the effect of scopolamine was similar with both auditory and visual CS modes. In the genetic line selected for low avoidance, and in the genetically heterogeneous line, the effects of the drug were different between the auditory and visual CS. It is suggested that scopolamine is more likely to disrupt responsiveness to visual stimuli, which have become less effective in the low avoidance line during the course of genetic selection. 5 references. (Author abstract)

001859 Schaefer, Gerald J.; Michael, Richard P. Michael: Georgia Mental Health Institute, 1256 Briarcliff Road, N.E., Atlanta, GA 30306 **Acute effects of neuroleptics on brain self-stimulation thresholds in rats.** *Psychopharmacology.* 67(1):9-15, 1980.

The acute effects of five neuroleptic drugs were tested in rats implanted with stimulating electrodes in the medial forebrain bundle and trained in a brain self-stimulation threshold procedure. Haloperidol (0.01 to 0.10mg/kg) and loxapine (0.03 to 0.56mg/kg) produced increases in reinforcement thresholds accompanied by reductions in response rates. Chlorpromazine

(0.10 to 3.0mg/kg) did not significantly alter reinforcement thresholds, but did produce dose dependent reductions in response rates. Pimozide (0.1 to 1.75mg/kg) was similar to chlorpromazine and significantly increased the reinforcement threshold only at the highest dose, although a graded decrease in response rates occurred over a wide dose range. Clozapine (0.1 to 1.75mg/kg) increased reinforcement thresholds without producing any significant changes in response rates, but when 3.0mg/kg of clozapine was administered, a marked disruption of behavior occurred. Results suggest that a distinction can be made between the effects of neuroleptics on motor behavior and on central reinforcement thresholds, and that this distinction may help in the interpretation of the relation between the chemical and clinical potency of antipsychotic drugs. 22 references. (Author abstract)

001860 Schallert, Timothy; De Ryck, Marc; Teitelbaum, Philip. Dept. of Psychology, University of Texas, Austin, TX 78712 **Atropine stereotypy as a behavioral trap: a movement subsystem and electroencephalographic analysis.** *Journal of Comparative and Physiological Psychology.* 94(1):1-24, 1980.

Movement subsystems involved in the stereotyped behaviors and electroencephalographic (EEG) activity that appear in rats given the anticholinergic drug atropine sulfate were analyzed. One form of stereotypy which occurs when drugged rats face the closed end of an alley for long periods of time was demonstrated to be alterable by merely changing the configuration of the environment. It appears that atropine produces an exaggerated snout thigmotaxis, and that alteration of the environment alters sensory input to the snout. Therefore, such stereotyped behavior is not a motor automatism but rather a circular chain of reflexive reactions to surfaces which trap the animal. During rapid shifts in direction of movement in undrugged rats, there were often extremely brief periods of hippocampal theta that could be blocked by atropine. The presence of theta during such shifts might be important for normal behavioral sequencing. This could partially account for the fact that atropine treated rats failed to change from their initial reactions in the alleyway to more adaptive behaviors. When a low roof was placed over the alleyway, head scanning was greatly limited, and immobility in a lying posture rapidly became the more frequent behavior. This immobility was accompanied by a sleep-like (synchronized) neocortical EEG pattern rather than the activated (desynchronized) neocortical pattern that occurs during repetitive thigmotactic scanning. It is hypothesized that scanning stereotypy and activated EEG are maintained through movement concurrent positive feedback. 59 references. (Author abstract modified)

001861 Schechter, Martin D. Dept. of Pharmacology, Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272 **Effect of neuroleptics and tricyclic antidepressants upon d-amphetamine discrimination.** *Pharmacology Biochemistry and Behavior.* 12(1):1-5, 1980.

After rats were trained to discriminate between the effects of intraperitoneal administration of 0.6mg/kg d-amphetamine and saline, the inhibitory effects on d-amphetamine discrimination of various neuroleptic and tricyclic antidepressants were investigated. Trifluoperazine, haloperidol, fluphenazine, chlorpromazine, and thioridazine, but not clozapine, decreased d-amphetamine-induced control of discriminative performance. The ED₅₀s of the effective neuroleptics for this inhibition were similar to those reported for antagonism of amphetamine-induced stereotypic behavior in the rat, and the slopes of the dose/response curves were parallel, indicating a common site and mechanism of action -- presumably blockade of postsynaptic dopaminergic receptors. In contrast, pretreatment with the tricyclic antidepressant agents, imipramine, nortryptiline, and desipramine

had no significant effect on the discrimination of a dose of d-amphetamine which produced a low degree of discriminative control. The results are viewed in relation to the dopamine hypothesis of schizophrenia and affective disorders, and the use of this animal behavioral method for determining brain dopamine interactions is discussed. 35 references. (Author abstract modified)

001862 Scherschlicht, R.; Bonetti, E. P.; Toh, C. C. Pharmaceutical Research Dept., F. Hoffman-La Roche & Co. Ltd., Basle, Switzerland **Effects of intracerebroventricularly injected on free behaviour and EEG activity of rats. A pilot study.** *Archives Internationales de Pharmacodynamie et de Therapie.* 239(2):221-229, 1979.

Nerveside, a phosphopeptide extracted from ox and dog brain, was injected unilaterally into the lateral ventricle of male rats prepared for EEG recording from the dorsal hippocampus and sensorimotor cortex. In doses of 150 and 300mcg, nerveside induced transient stereotyped behavior and longer lasting (about 3 hours) alterations of EEG activity and vigilance patterns. Wakefulness was increased and slow wave sleep and REM sleep were decreased. The vigilance pattern was characterized by rapid shifts between all three vigilance states. 6 references. (Author abstract modified)

001863 Schmidt, Hans, Jr. Dept. of Psychology, Xavier University, Victory Parkway, Cincinnati, OH 45207 **The effect of phenobarbital dose upon a variety of drinking related response measures.** *Pharmacology Biochemistry and Behavior.* 11(2):145-149, 1979.

Amount of water ingested, total laps, duration of drinking, amount per lap, laps per minute, and running velocity were investigated as a function of phenobarbital dosage (0 to 60mg/kg) in female rats deprived of water for 23.5 hours. Amount of water ingested, total laps, and duration of drinking all rose and subsequently fell as a function of dose on the day of drug treatment, rose as a linear function of dose a day later, and had no significant relation with dose 2 days later. These response measures significantly intercorrelated on the day of treatment and the day after, but not 2 days after. Running velocity largely declined as a function of dose on day of treatment but not thereafter. The other response measures showed no definite trends. However, running velocity, amount/lap and laps/minute intercorrelated on day of treatment but not thereafter. These two groups of measures did not consistently correlate with each other. 10 references. (Author abstract modified)

001864 Sclafani, Anthony; Eisenstadt, Donna. Dept. of Psychology, Brooklyn College, Brooklyn, NY 11210 **2-Deoxy-D-glucose fails to induce feeding in hamsters fed a preferred diet.** *Physiology & Behavior.* 24(3):641-643, 1980.

The feeding effects of 2-deoxy-D-glucose (2DG) in hamsters fed either lab chow alone or lab chow and sunflower seeds were examined. Hamsters fed a lab chow diet were found not to increase their food intake when injected with 2DG. The hamsters also failed to increase their intake of the preferred sunflower diet, following injections of 750 of 1.000mg/kg of 2DG. It is concluded that hamsters lack a glucoprivic feeding system. 20 references. (Author abstract modified)

001865 Sdraulig, R.; Rogers, L. J.; Boura, A. L. A. Pharmacology Dept., Monash University, Clayton, Victoria 3168, Australia **Glutamate and specific perceptual input interact to cause retarded learning in chicks.** *Physiology & Behavior.* 24(3):493-500, 1980.

The effects of the interaction between intracranial glutamate and specific perceptual input were examined with newly hatched chickens. It was found that for slowed visual learning

to be induced the chick needed to see intersecting lines, angles, or circles for 3 hours after glutamate administration on the second day of life. Stationary or moving lines were not effective. Slowed visual learning appeared to result from an interaction between glutamate and the neural activity resulting from exposure to patterned input and not the processes required for learning about the patterns. It is suggested that glutamate causes slowed visual learning by interfering with early forebrain development of higher visual areas which results from precise and specific changes in neural connectivity occurring in response to perceptual input. 40 references. (Author abstract modified)

001866 Seegal, Richard F.; Sikora, Edward; Hotchin, John. Division of Laboratories and Research, New York State Dept. of Health, Albany, NY 12201 **Locomotor effects of catecholaminergic drugs on herpes-infected mice.** *Pharmacology Biochemistry and Behavior.* 12(1):61-66, 1980.

Changes in spontaneous, amphetamine (AMP) and apomorphine (APO) induced locomotor activity were used to assess the effects of CNS infection with herpes type 1 virus. A dual herpes virus inoculation procedure was used in which the animals received an immunizing footpad inoculation followed at 2 weeks by an identical intracerebral challenge. Four weeks later the animals were tested with i.p. injections of saline of d-l-amphetamine. When footpad herpes virus was given via one or two injections it had no effect on spontaneous or AMP-induced activity. When footpad intracerebral herpes mice were tested 28 to 33 days postintracerebral inoculation, they demonstrated depressed AMP induced but not spontaneous activity. AMP at a dosage of 5.0mg/kg overcame the herpes virus blockage of 0.5 and 2.0mg/kg AMP-induced activity. Intraperitoneal injection of APO in day 3 postintracerebral animals produced less suppression of activity in the virus group than in the controls. These results suggest that nonfatal CNS herpes infection produces hypoactivity, in contrast to the hyperactivity during acute fatal CNS herpes encephalitis, and that the effect may be due to alterations in postsynaptic receptor sensitivity. It is noted that slowly acting viruses may be a significant cause of some human psychiatric disorders. 17 references. (Author abstract)

001867 Segal, David S.; Weinberger, Susan B.; Cahill, Jerome; McCunney, Stanley J. Dept. of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093 **Multiple daily amphetamine administration: behavioral and neurochemical alterations.** *Science.* 207(4433):904-907, 1980.

Behavioral and neurochemical alterations were observed in rats injected with 2.5mg/kg amphetamine every 4 hours for 5 days. A progressive augmentation in response occurred, characterized by a more rapid onset and an increased magnitude of stereotypy. By contrast, offset times of both the stereotypy and the poststereotypy hyperactivity periods were markedly shortened. When the animals were retested with the same dose of amphetamine 8 days after the long-term treatment was discontinued, the time of offset of the stereotypy and hyperactivity phases had recovered to values found with short-term amphetamine treatment, whereas the more rapid onset of stereotypy persisted. Brain monoamine and amphetamine concentrations and tyrosine hydroxylase activity were determined in comparably treated rats at times corresponding to the behavioral observations. The behavioral data indicate that enhanced responsiveness to amphetamine following its repeated administration may contribute to the development of amphetamine psychosis. 35 references. (Author abstract modified)

001868 Shapiro, Neil R.; Garg, Ajay P.; Riley, Edward P. Riley: Dept. of Psychology, State University of New York, Albany, NY 12222 **Genotypic-dependent amphetamine effects in**

rats bred for differences in alcohol sensitivity. *Physiological Psychology.* 7(4):403-406, 1979.

Locomotor activity in an open-field was assessed in two rat lines selectively bred for differences in alcohol sensitivity following an i.p. injection of 0, 1.5, or 3.0mg/kg d-amphetamine. The most affected (MA) line, bred for alcohol sensitivity, evidenced less of an increase in ambulation following amphetamine than did least affected (LA) rats, bred for alcohol insensitivity. Linear dose response functions with disparate slopes were found for the MA and LA rats, with activity of these lines becoming more divergent as dosage increased. Amphetamine increased rearing frequency in both lines, and though it appears that the LA line evidenced greater activation at the intermediate dose, this was not statistically significant. Amphetamine was also found to produce a dose dependent decrease in the duration of each rear, and this function appeared similar for the two lines. These data are compared to reports that inbred strains of mice which differ in sleep time following alcohol challenge also are distinguished in response to amphetamine. 17 references. (Author abstract modified)

001869 Sherman, A. D.; Allers, G. L. Neurochemistry Research Laboratory, Dept. of Psychiatry, University of Iowa, Iowa City, IA 52240 **Relationship between regional distribution of imipramine and its effect on learned helplessness in the rat.** *Neuropharmacology.* 19(2):159-162, 1980.

The regional distribution of imipramine and its major metabolite, desipramine, was determined in relation to drug effects in a learned helplessness paradigm. This model for depression has been shown to parallel the antidepressant action of imipramine in humans. Although 4 days of drug administration were required for a significant number of rats to show drug effects, some animals were responsive to a single dose of imipramine. Beginning with the first day, the desipramine levels in the hippocampi of animals in which imipramine prevented learned helplessness were significantly higher than in those animals which did not respond to imipramine. No such relationship was found for the other regions studied. The data suggest that the delay in onset of the effects of imipramine is related to the rate of hippocampal transport of its demethylated metabolite. 10 references. (Author abstract)

001870 Sherman, A. D.; Allers, G. L.; Petty, F.; Henn, F. A. Neurochemical Research Laboratories, Dept. of Psychiatry, University of Iowa, Iowa City, IA 52242 **A neuropharmacologically-relevant animal model of depression.** *Neuropharmacology.* 18(11):891-893, 1979.

The phenomenon of learned helplessness was evaluated as a potential animal model of depression. Lorazepam showed a protective effect on the development of this behavior in male Sprague-Dawley rats after single or repeated doses; imipramine showed a delayed protective effect with repeated doses, and chlorpromazine showed no protective effect. Dose/response curves related to the concentration of imipramine in drinking water or to free drug levels in brain were linear, with higher drug levels associated with a lowered degree of learned helplessness following chronic administration. The effects of imipramine were apparent after 4 days of access to the drug in drinking water, but not after 1, 2, or 3 days. It is concluded that this animal model does not provide a perfect fit with depression in humans but may be useful in studies of the mechanism of action of antidepressants. 14 references. (Author abstract modified)

001871 Silverman, Peter B.; Ho, Beng T. Texas Research Institute of Mental Sciences, 1300 Moursund Avenue, Houston, TX 77030 **Amphetamine discrimination: onset of the stimulus.** *Pharmacology Biochemistry and Behavior.* 12(2):303-304, 1980.

Rats were trained to discriminate 1.0mg/kg (-)-amphetamine sulfate from saline in a two lever operant procedure. The normal injection to session interval was 15 minutes. When tested with amphetamine immediately after intraperitoneal injection, rats initially responded on the lever paired with amphetamine training. When tested with saline immediately after injection, animals responded appropriately for the saline treatment throughout the extinction test. The results show that (-)-amphetamine exerts discriminative response control within 5 minutes of intraperitoneal injection. 10 references. (Author abstract)

001872 Slater, P.; Blundell, C.; Crossman, A. R. Dept. of Physiology, University of Manchester Medical School, Manchester M13 9PT, England **The effects of narcotic analgesics on the turning behaviour of rats with 6-hydroxydopamine-induced unilateral nigro-striatal lesions.** *Neuropharmacology*. 19(2):187-193, 1980.

The effects of narcotic analgesics on the turning behavior of rats with 6-hydroxydopamine-induced unilateral nigrostriatal lesions were investigated. Morphine at 5, 10, and 20mg/kg intraperitoneally caused a dose dependent, naloxone reversible, antagonism of d-amphetamine-induced ipsilateral circling in rats lesioned with 6-hydroxydopamine in one substantia nigra. Morphine (10mg/kg) weakly antagonized apomorphine-induced contralateral circling. Morphine, levorphanol, and phenazocine were potent antagonists of d-amphetamine-induced circling in rats with 6-hydroxydopamine lesion of one neostriatum. Pentazocine, pethidine, and ethylketocyclazocine were weak antagonists. It is proposed that a major action of morphine and some closely related opiate analgesics is to reduce the release of dopamine from nigrostriatal nerve terminals in the rat by acting upon specific opiate receptors. 33 references. (Author abstract modified)

001873 Slater, P.; Crossman, A. R. Dept. of Physiology, University of Manchester Medical School, Manchester M13 9PT, England **Effects of chronic morphine treatment on dopamine-mediated turning behaviour in rats and mice with 6-hydroxydopamine-induced unilateral nigro-striatal lesions.** *Neuropharmacology*. 19(3):289-295, 1980.

The effect of chronic morphine administration on dopamine stimulated circling behavior in rats and mice with unilateral lesions of nigrostriatal dopamine neurons was examined to investigate discrepancies in earlier research. Subcutaneous implantation of morphine tablets for 4 days was followed by naloxone precipitated morphine withdrawal on day 5. The results show that circling produced by the dopamine agonist apomorphine and by the indirectly acting agonist d-amphetamine is depressed in rats made tolerant to morphine. The same results were not observed in mice, and it is suggested that chronic morphine administration does not have the same effect in the striatum of rats and mice. The differences between the species are probably the result of the manner in which neurotransmitters are affected by morphine. 48 references. (Author abstract modified)

001874 Smith, Robert F. George Mason University, Fairfax, VA 22030 **Attenuation of septal lesion-induced shuttlebox facilitation by 5-hydroxytryptophan.** *Physiological Psychology*. 7(4):419-421, 1979.

Septal lesioned rats and unoperated controls were tested for acquisition of a shuttlebox avoidance task following saline or 5-hydroxytryptophan (5-HTP) injections. Septal animals with saline injections were significantly faster in learning the task. This facilitation was significantly attenuated by injections of 5-HTP. The data suggest that septal-lesion-induced shuttlebox facilitation may be a function of the serotonin reduction previous-

ly reported to be a consequence of the lesion. 11 references. (Author abstract modified)

001875 Souto, Mario; Frances, Henriette; Lecrubier, Yves; Puech, Alain J.; Simon, Pierre. Dept. of Pharmacologie, Faculté de Médecine Pitié-Salpêtrière, 91, blvd. de l'Hôpital, F-75634 Paris, Cedex 13, France **Antagonism by d,l-propranolol of imipramine effects in mice.** *European Journal of Pharmacology*. 60(1):105-108, 1979.

Imipramine, salbutamol, and dexamphetamine were active in several animal tests predictive of antidepressant activity in man, including potentiation of yohimbine-induced toxicity and antagonism of hypothermia induced by reserpine, oxotremorine, or a high dose of apomorphine. These effects were antagonized by d,l-propranolol, suggesting the stimulation of beta-adrenergic receptors could be a common mechanism of action for these antidepressant drugs. These findings are consistent with the noradrenergic hypothesis of the pathophysiology of affective disorders. 4 references. (Author abstract modified)

001876 Squire, Larry R. Veterans Administration Hospital, San Diego, CA 92161 **Cerebral protein synthesis inhibition and discrimination training: effects of D-amphetamine.** *Brain Research*. 177(2):401-406, 1979.

The effects of d-amphetamine on the amnesia produced by protein synthesis inhibition were examined in male Swiss mice. D-amphetamine reversed amnesia induced by the protein synthesis inhibitor cycloheximide (CXM). This effect was due to facilitation of performance during retention testing rather than to specific improvement in retrieval of previously unavailable information. Results indicate that CXM interferes with the formation of long-term memory rather than with the retrieval process. 19 references.

001877 St. John, A. B.; Born, C. K. Dept. of Pharmacal Sciences, School of Pharmacy, Auburn University, Auburn, AL 36830 **Characterization of analgesic and activity effects of methotrimeprazine and morphine.** *Research Communications in Chemical Pathology and Pharmacology*. 26(1):25-34, 1979.

The interactions of methotrimeprazine (MTM) with naloxone, morphine, and central opiate receptors were examined in male Swiss mice. MTM (16 to 256nM) did not compete with tritiated naloxone for specific binding sites in mouse brain homogenates. In vivo, -MTM-induced analgesia was not antagonized by naloxone. After 14 days administration of MTM, partial tolerance developed to the sedative effects of the drug, but not the analgesic effects. Chronic treatment with morphine led to tolerance to its effects on activity as well as pain perception. Results suggest that the analgesic effects of MTM and morphine are not mediated by the same mechanisms. 10 references. (Author abstract modified)

001878 Standridge, R. T.; Howell, H. G.; Tilson, H. A.; Chamberlain, J. H.; Holava, H. M.; Glyls, J. A.; Partyka, R. A.; Shulgin, A. T. Research Division, Bristol Laboratories, Division of Bristol-Myers Company, Syracuse, NY 13201 **Phenylalkylamines with potential psychotherapeutic utility.** *Journal of Medicinal Chemistry*. 23(2):154-162, 1980.

In a study to further explore phenylalkylamines with potential psychotherapeutic utility, a series of 2-amino-1(4-substituted-2,5-dio,etjxypehnyl) butanes were prepared as analogues of (R)-2-amino-1-(2,5-dimethoxy-4-methylphenyl) butane. 1-(2,5-dimethoxyphenyl)-2-(N-phthalimido) butane was utilized as a synthetic intermediate common to many of the target compounds. Animal data are presented indicating that most of these analogues have low hallucinogenic potential. Selected compounds were compared with (R)-2-amino-1-(2,5-dimethoxy-4-methylphenyl)

butane in an avoidance response acquisition model which differentiates between that compound and the human hallucinogens DOM and DOET. Structure activity relationships of these analogues are discussed. 21 references. (Author abstract modified)

001879 Stapleton, June M.; Merriman, Vicki J.; Coogle, Constance L.; Gelbard, Steven D.; Reid, Larry D. Rensselaer Polytechnic Institute, Troy, NY 12181 **Naloxone reduced pressing for intracranial stimulation of sites in the periaqueductal gray area, accumbens nucleus, substantia nigra, and lateral hypothalamus.** *Physiological Psychology*. 7(4):427-436, 1979.

The effects of naloxone and morphine on self-stimulation of sites in the periaqueductal gray area, accumbens nucleus, substantia nigra, and lateral hypothalamus were investigated in rats. After stabilization of press rates, Ss were tested under morphine, naloxone, or placebo. Morphine sulfate, with testing 3 hours after injection, produced an increase in press rates at all sites tested. Naloxone hydrochloride, given immediately before testing, produced reliable reductions in press rates in a 50 to 60 minute test at all four sites. The same dose of naloxone, given 15 minutes before a 3 minute test, produced a small, but reliable, reduction in pressing for intracranial stimulation of the lateral hypothalamus. Results suggest that endorphin systems play a modulatory role in pressing for intracranial stimulation. 29 references. (Author abstract modified)

001880 Steinfels, G. F.; Young, G. A.; Khazan, N. University of Maryland School of Pharmacy, Dept. of Pharmacology and Toxicology, Baltimore, MD 21201 **Opioid self-administration and REM sleep EEG power spectra.** *Neuropharmacology*. 19(1):69-74, 1980.

Changes in power spectra derived from successive REM sleep EEG episodes during self-administration of morphine, methadone, 1-alpha-acetylmethadol (LAAM), nor-LAAM, and dinor-LAAM were studied in female Sprague-Dawley rats. During self-administration of these narcotic drugs, the first REM sleep episode following an injection had a faster peak EEG frequency. Peak EEG frequencies of the successive REM sleep episodes during an interinjection interval declined in a linear fashion. Differences in the slopes of the linear peak EEG frequency declines of the different drugs correlated with differences in their pharmacokinetic profiles. The slowing in peak EEG frequencies may reflect a decline in brain levels of the respective drug, leading to changes in the CNS that precede drug seeking behavior. 35 references. (Author abstract modified)

001881 Stevens, David R.; Klemm, W. R. Dept. of Biology, Texas A & M University, College Station, TX 77843 **Morphine-naloxone interactions: a role for nonspecific morphine excitatory effects in withdrawal.** *Science*. 205(4413):1379-1380, 1979.

The role for nonspecific morphine excitatory effects in withdrawal was investigated. The opiate antagonist naloxone precipitates withdrawal when given either 15 minutes after or 1 minute before a single injection of morphine in drug naive mice. It is proposed that withdrawal signs arise from a synergistic mixture of excitatory influences that are direct (agonist action on nonspecific opiate receptors) and indirect (sensory and affective disorders, stress, hormonal and neurotransmitter dysfunction and so forth). The predominant effects during precipitated withdrawal are assumed to be direct, whereas during abstinence in tolerant animals they are indirect. 15 references. (Author abstract modified)

001882 Sturgeon, R. David; Fessler, Richard G.; Meltzer, Herbert Y. Laboratory of Biological Psychiatry, Illinois State Psychiatric Institute, Chicago, IL **Behavioral rating scales for assessing phencyclidine-induced locomotor activity, stereotyped behavior**

and ataxia in rats. *European Journal of Pharmacology*. 59(3/4):169-179, 1979.

Behavioral rating scales were developed for quantification of phencyclidine (PCP) induced locomotor activity, stereotyped behavior, and ataxia in male Sprague-Dawley rats. The dose/response relationship for locomotor activity during a 90 minute period following PCP administration was an inverted U-shaped function for the first 25 minutes and a linear function for the last 30 minutes. A linear dose/response relationship was found for ratings of stereotyped behavior and ataxia throughout the 90 minute period. The effects of PCP on locomotor activity were greatest during intervals when stereotyped behavior and ataxia were at moderate levels. Ratings of locomotor activity may be confounded by ataxia when PCP is given alone or in combination with other drugs. 26 references. (Author abstract modified)

001883 Svare, Bruce B. State University of New York, Albany, NY 12222 **Hormonal influences on pup-killing behavior in mice.** (Unpublished paper). Final Report, NIMH Grant R03-MH-32467, 1979. 7 p.

The effectiveness of the hormones estrogen and aromatizable and nonaromatizable androgens in the organization and activation of pup killing behavior in mice was examined in two series of experiments. In the first series, the activation of pup killing behavior was examined in ovariectomized adult female mice treated with oil, estradiol benzoate, testosterone, androstenedione, androstenedione, dihydrotestosterone, or combinations of these steroids. In the second series, the organization of pup killing behavior was examined in neonatally ovariectomized female mice treated at the time with a single injection of oil or one of the steroids of the first series of experiments, and treated in adulthood with an injection of testosterone. The data suggest that aromatization of testosterone to estrogen may be important for the organization and activation of pup killing behavior. 2 references.

001884 Svare, Bruce. Dept. of Psychology, State University of New York, 1400 Washington Ave., Albany, NY 12222 **Testosterone propionate inhibits maternal aggression in mice.** *Physiology & Behavior*. 24(3):435-439, 1980.

The effects of testosterone propionate (TP) on maternal aggression in lactating mice were examined with Rockland-Swiss albino mice. Daily injections of TP significantly decreased the number of attacks exhibited by lactating female mice toward male intruders. Treatment with TP also depressed the body weights of the dams as well as their lactation performance but these effects were observed long after deficits in aggression were noted. The question remains as to whether or not the observed inhibitory effect of TP on maternal aggressive behavior is a pharmacological one, or whether endogenous circulating levels of testosterone might normally inhibit the behavior. 29 references. (Author abstract modified)

001885 Tabakoff, Boris; Ritzmann, R. F.; Oltmans, Gary A. Dept. of Physiology and Biophysics, University of Illinois Medical Center, Chicago, IL 60612 **The effect of selective lesions of brain noradrenergic systems on the development of barbiturate tolerance in rats.** *Brain Research*. 176(2):327-336, 1979.

The importance of noradrenergic systems in the development of barbiturate tolerance was studied in male Sprague-Dawley rats, using a newly developed method for chronic infusion of barbiturates into the CNS. Measurements of righting reflex, body temperature, and brain barbiturate levels in response to a challenge dose of sodium pentobarbital (10mg/kg i.p.) 24 hours after the termination of 72 hour intraventricular infusion of sodium phenobarbital or vehicle revealed a functional tolerance to barbiturates in the sodium phenobarbital treated rats. The de-

velopment of barbiturate tolerance was prevented by destruction of the noradrenergic neurons with intraventricular 6-hydroxydopamine or by specific lesions of the dorsal or ventral noradrenergic bundles. The animals' response to acute administration of barbiturate was not altered by these lesions. 22 references. (Author abstract modified)

001886 Taylor, Dorothy; Ho, Beng T. Texas Research Institute of Mental Sciences, Houston, TX 77030 **The role of serotonin in cocaine-induced hypermotility in rats.** Research Communications in Psychology, Psychiatry and Behavior. 4(4):447-456, 1979.

The relationship between serotonin function and cocaine-induced hypermotility was investigated. Increased levels of serotonin by either pretreatment with 5-hydroxytryptophan or feeding with a carbohydrate diet resulted in a blockade of cocaine-induced locomotor stimulation of rats. The diet also attenuated, although to a lesser extent, the hypermotility response of animals injected with amphetamine, but had no effect on methylphenidate treated rats. Biochemical measurement of serotonin turnover was included to explain the role of serotonin in the stimulant property of cocaine. 20 references. (Author abstract modified)

001887 Teitelbaum, Herman; Giammatteo, Paul; Mickley, G. Andrew. Behavioral Sciences Department, Armed Forces Radiology Research Institute, Bethesda, MD 20014 **Differential effects of localized lesions of the n. accumbens on morphine- and amphetamine-induced locomotor hyperactivity in the C57BL/6J mouse.** Journal of Comparative and Physiological Psychology. 93(4):745-751, 1979.

Differential effects of localized nucleus accumbens lesions on morphine and amphetamine-induced locomotor hyperactivity were examined in the C57BL/6J mouse. Mice became hyperactive to increasing doses of morphine sulphate. This response was similar to locomotor hyperactivity induced by amphetamine. Lesions and chemical blockade of the posterior nucleus accumbens abolished amphetamine-induced hyperactivity and reduced, but did not abolish, the morphine response. Findings demonstrated that the response to the two drugs is mediated by overlapping but noncongruent neural systems. 18 references. (Author abstract modified)

001888 Thiebot, Marie-Helene; Kloczko, Joseph; Chermat, Raymond; Simon, Pierre; Soubrie, Philippe. Simon: Dept. de Pharmacologie, Faculte de Medecine Pitie-Salpetriere, 91, boulevard de l'Hopital, F-75634 Paris, Cedex 13, France **Oxolinic acid and diazepam: their reciprocal antagonism in rodents.** Psychopharmacology. 67(1):91-95, 1980.

The stimulant effects of oxolinic acid were investigated in rats and mice. This drug, given orally, constantly induced, in doses ranging from 16 to 250mg/kg, locomotor stimulation and stereotyped behavior. These effects were antagonized by pimoide, alpha-methyltyrosine, or reserpine pretreatment, suggesting a facilitatory role of oxolinic acid on catecholaminergic processes. Diazepam reduced the stimulant effects induced by oxolinic acid but not those induced by amphetamine; oxolinic acid markedly reduced the antipunishment effect elicited in rats by diazepam. Since benzodiazepines have been reported to enhance GABA functioning, these data suggest that oxolinic acid may impair GABA transmission. However, neither muscimol nor gamma-aminobutyric acid selectively reduced the stimulant effects elicited by oxolinic acid. Therefore, the possible facilitation exerted by this drug on catecholaminergic systems may not derive from the release of an inhibitory GABAergic control. 22 references. (Author abstract modified)

001889 Thompson, Donald M.; Moerschbaecher, Joseph M. Department of Pharmacology, Georgetown University Schools

of Medicine and Dentistry, Washington, DC 20007 **An experimental analysis of the effects of d-amphetamine and cocaine on the acquisition and performance of response chains in monkeys.** Journal of the Experimental Analysis of Behavior. 32(3):433-444, 1979.

The effects of varying doses of d-amphetamine and cocaine on the acquisition and performance of response chains in monkeys were investigated, and learning and performance conditions were compared within each session using a multiple schedule. Possible behavioral mechanisms for the drug effects were also sought. Both drugs disrupted behavior in the learning component at higher doses. The performance component was generally less sensitive to disruption. When the four discriminative stimuli in both components were removed, however, behavior was disrupted more in the performance component. It is concluded that the greater sensitivity of the learning component to disruptive drug effects is related to the relatively weak stimulus control and/or the lower rate of reinforcement associated with that component. 19 references. (Author abstract modified)

001890 Thompson, Donald M.; Moerschbaecher, Joseph M. Dept. of Pharmacology, Georgetown University Schools of Medicine and Dentistry, Washington, DC 20007 **Effects of d-amphetamine and cocaine on strained ratio behavior in a repeated-acquisition task.** Journal of the Experimental Analysis of Behavior. 33(1):141-148, 1980.

Whether different drug effects would be found in pigeons if behavior was maintained under larger fixed ratio schedules than those employed in previous research was examined. When the fixed ratio requirement for food presentation was five completions of a four response chain, d-amphetamine and cocaine disrupted the behavior. As the dose of each drug was increased, the overall response rate decreased, the overall accuracy was impaired, and there was less within session error reduction. In contrast, when the fixed ratio requirement was either 20 or 50 completions of the chain, certain doses of both drugs produced large increases in the overall response rate by eliminating the extended pausing that was characteristic of the control sessions. These rate increasing effects were accompanied by error decreasing effects, both during acquisition and after the response chain had been acquired. Taken together, the results indicate that the effects of d-amphetamine and cocaine on behavior in a repeated acquisition task can be modulated by manipulating the value of the fixed ratio schedule maintaining the behavior. 15 references. (Author abstract modified)

001891 Thompson, Richard W. Western Washington University, Bellingham, WA 98225 **Comments on Ksir, C. Immobility in chickens.** Physiological Psychology. 7(4):454-455, 1979.

The finding reported by Ksir (1978) that scopolamine does not reduce tonic immobility in chickens is disputed, and four areas in which Ksir did not replicate the study he claimed to have replicated are discussed. These four areas include: 1) use of different strain experimental Ss, 2) procedures for summation of data from several trials, 3) use of unorthodox testing procedures, and 4) confusion concerning the criteria for distinguishing between an activity box and the open-field. 8 references.

001892 Thompson, Richard W.; Jensen, Dan. Western Washington University, Bellingham, WA 98225 **Adrenergic and cholinergic systems and tonic immobility in chickens.** Bulletin of the Psychonomic Society. 14(6):467-468, 1979.

To investigate the possible interaction of adrenergic and cholinergic systems in the mediation of tonic immobility (TI) in chickens, 40 cockerel chicks were divided into two groups that received .5mg/kg or 1mg/kg of epinephrine. Half of each of these groups were given 1mg/kg or 2.5mg/kg of scopolamine

prior to testing for TI duration. Results indicate that the highest dose of epinephrine significantly increased TI duration. Although the highest dose of scopolamine attenuated the duration of TI at both epinephrine levels, the effect was not significant. 11 references. (Author abstract)

001893 Thompson, William R.; Wright, Janet S. Queen's University at Kingston, Kingston, Ontario, Canada *Physiological Psychology*. 7(3):291-294, 1979.

Two experiments designed to examine further the reported effect of the steroid hormone testosterone on persistence are presented. Persistence was defined in terms of difficulty of shifting from one discrimination habit to a new one in which previously relevant dimensions now were irrelevant. In the first study, adult male rats injected with a moderate dosage level of testosterone showed increased persistence compared with oil injected and androsterone injected groups and with animals receiving a high dosage of testosterone. In a second study, male rats injected with the antiandrogen cyproterone acetate showed a reduction in persistence compared with controls. In both experiments, arousal levels were measured by nonreinforced barpress rates during and between trials. In neither study were differences in arousal level relevant to the drug effects. The results are in general agreement with those of other workers using chicks and mice. 11 references. (Author abstract)

001894 Thorn, Beverly E.; Levitt, R. A. Levitt: Dept. of Psychology, University of Alabama in Birmingham, Birmingham, AL 35294 *Etorphine induction of analgesia and catatonia in the rat: systemic or intracranial injection*. *Neuropharmacology*. 19(2):203-207, 1980.

Etorphine induction of analgesia and catatonia in the rat were investigated. Etorphine was injected into the rat either intraperitoneally or by microinjection in the periaqueductal gray (PAG) region of the midbrain, or in the cerebellum (CB). The flinch jump technique was used to measure analgesia and the bar test to assess catatonia. Etorphine doses were 5, 10, 50, or 100 micrograms/kg. The doses of etorphine administered to the PAG were 0.1, 1.0, 2.0, or 3.0 micrograms. The dose of etorphine administered to the cerebellum was 2.0 micrograms. The effective doses into the PAG for producing both analgesia and catatonia were about 15 times less than the intraperitoneal doses, suggesting central mediation of these actions, involving the PAG and perhaps other CNS sites. Injection of 2.0 micrograms etorphine into the cerebellum did not cause analgesia or catatonia. There was a high correlation between the production of analgesia and of catatonia suggesting a common factor in these actions, at least as measured in this study. 21 references. (Author abstract modified)

001895 Tissot, Rene. Clinique psychiatrique de Geneve, CH-1225 Chene-Bourg, Switzerland *Opiate receptors and sleep. I. Effects of microinjections of morphine in the median thalamus and the periaqueductal gray matter of the rabbit. Recepteurs a opiaces et sommeil: I. Effets de micro-injections de morphine dans le thalamus median et la substance grise centrale periaqueductale du lapin*. *Neuropsychobiology*. 6(3):170-179, 1980.

The effects of microinjections of morphine in the median thalamus and the periaqueductal gray matter of the rabbit on sleep and analgesia were investigated. Microinjections in optimal doses into the median thalamus (40mcg) and periaqueductal gray matter (10 to 20mcg) produced slow wave sleep with abundant spindles, in addition to analgesia. Like analgesia, the sleep inducing effect is blocked by naloxone. It is concluded that the effect is related to the agonistic action of morphine on endorphin receptors. It is probable that the endorphins constitute a regulatory system acting on the medullary/thalamic sleep

inducing structures which generate the sleep spindles. At higher dose levels, injections of morphine into the same structures produce behavioral agitation resembling the dissociated REM sleep described by Jouvet, which is not blocked by naloxone. The agitation might be due to an indirect action of morphine, and therefore of endorphin receptors, acting on monoaminergic structures. 56 references. (Author abstract modified)

001896 Turkelson, Charles Mathew. Tulane University *Brain estrogen receptor dynamics, sexual receptivity and aging*. (Ph.D. dissertation). Dissertation Abstracts International. 39(11):5630-B, 1979. Ann Arbor, Univ. Microfilms No. 7910258, 73p., 1978.

Nuclear and cytosol hypothalamic and amygdaloid estrogen receptors were simultaneously assayed in 60-day-old, 200-day-old, and 475-day-old, 1 week ovariectomized female rats at 0, 1.5, and 6 hours after estradiol injection regimes which either did or did not induce sexual receptivity. Results suggest that the amygdala and hypothalamus respond differently to estrogen and that the amount of estrogen receptors retained in hypothalamic cell nuclei covaries directly with the degree of sexual behavior manifested in young and aging rats. It is suggested that estradiol induced cytosol estrogen receptor synthesis in the long-term but not in the short-term castrate and that differences in nuclear events may exist between the two preparations. (Journal abstract modified)

001897 Tyler, Julia L.; Gorski, Roger A. Dept. of Biological Sciences, Northwestern University, Evanston, IL 60202 *Bulbectomy and sensitivity to estrogen: anatomical and functional specificity*. *Physiology & Behavior*. 24(3):593-600, 1980.

The influence of the olfactory system on female sexual behavior was examined in ovariectomized rats given sham operations (SHAM), total bilateral olfactory bulbectomy (TBULBX), partial bulbectomy (PBULBX), anterior olfactory nucleus lesions (AON), or accessory olfactory bulb lesions (AOB) and tested for lordosis behavior. Only TBULBX resulted in increased sensitivity to estradiol benzoate (EB). Only TBULBX rats were anomic on two postoperative tests. Bulbectomy-induced alterations in sensitivity to EB as measured by lordosis behavior do not appear to be due to alterations in arousal mechanisms in general. It is concluded that bulbectomy may enhance behavioral sensitivity to EB by disrupting biochemical responses to EB in limbic system structures which normally exert an inhibitory influence over sexual receptivity. 57 references. (Author abstract modified)

001898 Valliant, Paul M.; Persinger, Michael A.; Satinder, K. Paul. Dept. of Psychology, St. Mary's University, Halifax, Nova Scotia, Canada B3H 3C3 *Long-term effects of preweaning taurine injections in rats*. *Developmental Psychobiology*. 12(5):515-518, 1979.

MR, MNR, and RCA strains of rats that had been injected with either 62.5mg/kg of taurine or comparable volumes of physiological saline between postnatal days 8 and 20 and later tested at 100 days of age in an open-field and one way shock avoidance situations, are presented. Taurine injected rats displayed significant elevation in defecation score in the open-field. In addition, a significant treatment x strain interaction was due to the larger defecation numbers displayed by the taurine injected MR rats relative to the saline injected MR rats. 5 references. (Author abstract modified)

001899 van Dongen, P. A. M. Dept. of Pharmacology, University of Nijmegen, P.O.B. 9101, 6500 HB Nijmegen, The Netherlands *Locus coeruleus region: effects on behavior of cholinergic, noradrenergic, and opiate drugs injected intracerebrally into freely moving cats*. *Experimental Neurology*. 67(1):52-78, 1980.

Behavioral effects of intracerebral injections of small amounts of cholinergic, noradrenergic, and opiate agents into 125 sites in and around the locus ceruleus of the cat were investigated. Carbachol caused atonia comparable to the atonia during paradoxical sleep; the most effective regions were the nucleus pontis centralis caudalis and the subceruleus region. Carbachol injected into the nucleus pontis centralis oralis caused defense reactions like hissing and growling and disturbed vocalizations. Micturition and defecation were elicited by carbachol injected near the nucleus laterodorsalis tegmenti. Carbachol caused ipsiversive and contraversive circling when injected in or near the region of the norepinephrine containing cell bodies; this circling was probably not due to the NE cells. Alpha-noradrenergic and opiate agonists injected into the part of the nucleus pontis centralis oralis just rostral to the locus ceruleus caused behavioral inactivation. Alpha-noradrenergic agonists caused vomiting; the most effective region was the fourth ventricle. Naloxone injected intracerebrally in morphine treated cats antagonized the morphine-induced stereotyped behavior. It is suggested that the locus ceruleus acts as a sympathetic nucleus situated in the brain with extensive parts of the central nervous system as its target regions. 68 references. (Author abstract modified)

001900 Velasco, Francisco; Velasco, Marcos; Maldonado, Hector; Romo, Ranulfo; Estrada-Villanueva, Francisco. Division of Neurophysiology, Scientific Research Department, National Medical Center, I.M.S.S., Mexico City, Mexico **Specific and nonspecific multiple unit activities during the onset of pentylenetetrazol seizures. III. Animals with ablations of the cerebral cortex.** *Epilepsia*. 20(6):635-642, 1979.

The effects of cortical ablations on behavior, wakefulness/sleep states, and pentylenetetrazol (PTZ) induced seizures were studied in a group of cats. Animals with ablations of primary sensory cortices showed apathy, decreased visual and auditory reactivity, and postural defects, but no significant changes in sleep/wakefulness states. Threshold doses of PTX failed to induce EEG tonic/clonic discharges but did increase multiple unit activity (MUA) of the motor cortex and the mesencephalic and pontine reticular formations, as has been reported for intact animals. In contrast, animals with ablations of association cortices showed variable degrees of hyperactivity, significant increase in the amount of wakefulness and decrease in slow wave sleep with no changes in paradoxical sleep. Threshold doses of PTZ-induced EEG tonic/clonic seizures that lasted 10 to 100 times as long as those seen in intact animals, and MUA increments of the motor cortex and mesencephalic and pontine reticular formations were significantly larger than those observed in animals with ablations of primary sensory cortices or intact animals. Findings suggest that association cortices modulate the wakefulness/sleep states and exert an important inhibitory effect on the development of PTZ-induced seizure activity at cortical and subcortical levels. 26 references. (Author abstract modified)

001901 Vergnes, Marguerite; Bandler, Richard; Kempf, Eliane. Laboratoire de Neurophysiologie, Centre de Neurochimie du CNRS, 11, rue Humann, 67000 Strasbourg, France **Muricide induced by diagonal band damage: role of 5-HT pathways.** *Brain Res.* 185(1):203-207, 1980.

The role of serotonergic pathways in the muricide induced by damage to the diagonal band was examined. The neurotoxin 5,7-dihydroxytryptamine (5,7-DHT) was injected bilaterally into the region of the vertical limb of the diagonal band of Broca in 28 male Wistar rats. A 74% reduction in serotonin (5-HT) content was observed in the hippocampus and cortex of these animals, and no other damage to the diagonal band or septum was observed. Muricidal behavior occurred with the same frequency in rats treated with 5,7-DHT as in controls. Results indicate that muricidal behavior observed after damage to the diagonal

band is not solely dependent on changes in 5-HT in the hippocampus and cortex. 27 references.

001902 Vetulani, J.; Bednarczyk, Barbara; Reichenberg, Krystyna; Rokosz, Anna. Institute of Pharmacology, Polish Academy of Sciences, 31-343 Krakow, Poland **Head twitches induced by LSD and quipazine: similarities and differences.** *Neuropharmacology*. 19(2):155-158, 1980.

Intraperitoneal injections of LSD and quipazine produced head twitches in the rat. The dose/response curves were bell shaped, with maxima at 50 micrograms/kg for LSD and 5 mg/kg for quipazine. In a single animal the responses to two consecutive treatments with the same agent were similar, and the correlations between the responsiveness to LSD and quipazine were high. Head twitches induced by LSD were inhibited more strongly than those observed after quipazine by drugs impairing noradrenergic transmission and by morphine. The converse was true for a serotonin antagonist, cyproheptadine, and for morphine derivatives, particularly N-cyclopropylmethyl norazidomorphine. Results suggest an involvement of the central noradrenergic system in the response to LSD in addition to a serotonergic mechanism, and auxiliary participation of one kind of opiate receptors in the action of quipazine. 24 references. (Author abstract)

001903 vom Saal, Frederick S. Institute of Reproductive Biology, Zoology Department, University of Texas, Austin, TX 78712 **Prenatal exposure to androgen influences morphology and aggressive behavior of male and female mice.** *Hormones and Behavior*. 12(1):1-11, 1979.

The effects of prenatal exposure to androgen on adult aggressiveness in mice were assessed. Pregnant mice were given injections of 1.5 mg testosterone propionate (TP) or oil from days 12 to 16 of pregnancy. All offspring were gonadectomized on the day of birth. Neonatal treatment occurred on the day following birth and consisted of one half of the mice from each prenatal treatment group being injected with TP while the other half was injected with oil. On postnatal day 60, all offspring were given subcutaneous implants of encapsulated testosterone and tested for 10 min every other day against a male opponent until aggression was observed. Results show that morphological and behavioral masculinization can occur in mice in response to exposure to androgen during prenatal as well as neonatal life. 19 references. (Author abstract modified)

001904 Waddington, John L. Division of Psychiatry, MRC Clinical Research Centre, Watford Road, Harrow, Middlesex, HA1 3UJ, England **A methodological weakness in the use of neuroleptic antagonism as a sole criterion for Daergic mediation of drug-induced behavioural effects.** *European Journal of Pharmacology*. 58(3):327-329, 1979.

Unilateral injections of the GABA agonist muscimol (100 ng) or the GABA analogue baclofen (1 mcg) into the zona reticulata of the substantia nigra produced contralateral rotation in male Sprague-Dawley rats. The drug-induced rotation was attenuated by pretreatment with haloperidol (0.4 mg/kg i.p.), but not by destruction of ipsilateral dopamine (DA) neurons with 6-hydroxydopamine. It is concluded that neuroleptic antagonism of drug-induced behavioral effects can erroneously indicate the involvement of striatal dopaminergic mechanisms, due to nonspecific and extrastriatal actions of the neuroleptics. 10 references. (Author abstract modified)

001905 Walker, William A.; Feder, H. H. Feder: Rutgers University, Institute of Animal Behavior, 101 Warren St., Newark, NJ 07102 **The comparative potency of various steroids to complete the priming process for lordosis in guinea pigs.** *Hormones and Behavior*. 12(3):299-308, 1979.

A series of experiments was conducted to determine whether the differences between the estrogenic actions of enclomiphene and estradiol benzoate (or the unesterified form) are due to quantitative or qualitative factors. Ovariectomized adult guinea-pigs were treated with a regimen of estradiol benzoate that was shown to be minimally effective for the induction of lordosis. They were then treated with 10, 20, or 80mg of enclomiphene; 5, 20, 50 or 100mcg of estradiol; or testosterone, corticosterone, estrone, estril, diethylstilbestrol, catechol estradiol, or catechol estrone at hour 28. At hour 39 all females were given 0.5mg progesterone, and subsequently tested for lordosis behavior. Of the various agents injected at hour 28, only estradiol (at all doses given), estrone, estril, and diethylstilbestrol were effective in supporting display of lordosis behavior. The results indicate that the antiestrogen enclomiphene, the catechol estrogens, and at least some C19 and C21 steroids are weaker than E2 or ineffective in facilitating lordosis behavior when given late in the priming period. Because previous work had shown that enclomiphene has partial estrogenic effects on lordosis behavior when administered early in the priming period, it is suggested the early and late phases of the priming process induced by E2 entail qualitatively different neural processes. 10 references. (Author abstract modified)

001906 Wauquier, A.; Niemegeers, C. J. E. Dept. of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **A comparison between lick or lever-pressing contingent reward and the effects of neuroleptics thereon.** Archives Internationales de Pharmacodynamie et de Therapie. 239(2):230-240, 1979.

The effects of neuroleptics on intracranial self-stimulation were examined in male Wistar rats trained to obtain stimulation of the lateral hypothalamus by pressing a lever or by licking a steel drinking tube. Haloperidol, pimozide, pipamperone, and azaperone produced a dose related inhibition of licking for brain stimulation, but suppressed lever-pressing only at the highest dose tested. This differential sensitivity to neuroleptics appeared to be due to different thresholds of reinforcement produced by licking and lever-pressing for brain stimulation. 21 references. (Author abstract modified)

001907 Weiner, William J.; Carvey, Paul M.; Nausieda, Paul A.; Klawans, Harold L. Dept. of Neurological Sciences, Rush-Presbyterian-St. Luke's Medical Center, 1725 West Harrison St., Chicago, IL 60612 **Dopaminergic antagonism of L-5-hydroxytryptophan-induced myoclonic jumping behavior.** Neurology. 29(12):1622-1625, 1979.

The effect of the dopamine agonists, levodopa, apomorphine, lergotril, and 2(dimethylamino)5,6-dihydroxytetralin (M-7) on myoclonic jumping behavior was examined in young male guinea pigs. All these agents had a significant effect on the frequency of this serotonin mediated behavior. The duration of the antagonism corresponded in all cases to the duration of the stereotyped chewing behavior induced by these agents alone. The dopamine antagonist, haloperidol, potentiated jumping behavior. Therefore, myoclonic jumping behavior is influenced by dopaminergic mechanisms and this behavior may be the result of the interaction between dopaminergic and serotonergic activity. It is concluded that the role of dopaminergic mechanisms in human myoclonic disorders needs further clarification. 19 references. (Author abstract)

001908 Weiss, Bernard; Wood, Ronald W.; Macys, David A. Dept. of Radiation Biology and Biophysics, University of Rochester Medical Center, Rochester, NY 14642 **Behavioral toxicology of carbon disulfide and toluene.** Environmental Health Perspectives. 30:39-45, 1979.

Data on the actions of carbon disulfide and toluene in the squirrel monkey were obtained from a situation designed to determine aversive thresholds to electrical stimulation. Effective concentrations of carbon disulfide produced both a rise in the amount of electrical shock tolerated and a diminution of the response force exerted by the monkeys. In experiments with toluene, pigeons were shown to elevate key-pecking rate in an operant situation at certain concentrations. Toluene was also studied for its capacity to maintain self-administration in the same way as drugs of abuse. Monkeys worked to gain access to toluene vapor just as they work for opiates or amphetamines. The current experiments demonstrate how comprehensive the range of behavioral toxicology needs to be to deal with environmental health issues. 31 references. (Author abstract modified)

001909 Wells, Maria J.; Cole, Sherwood O. Rutgers University, Camden, NJ 08102 **The noneffect of lesions of the corpus striatum upon amphetamine-induced stereotypy.** Bulletin of the Psychonomic Society. 14(6):407-409, 1979.

Stereotyped behavior produced by d-amphetamine in male Holtzman rats with electrolytic lesions of the corpus striatum was compared with that produced in striatal sham operated and normal controls. While ratings of behavior over three test sessions demonstrated a highly significant drug dose effect, amphetamine-induced stereotypy in the striatal lesion group did not differ significantly from that observed in the other two groups. These findings are discussed in reference to the importance of degree of striatal damage, time after surgery, and the proposed role of other dopaminergic sites to the mediation of the drug's effect. The need for a critical examination of all experimental contingencies surrounding the proposed mediational role of the striatum is also emphasized. 15 references. (Author abstract)

001910 Westenberg, Irwin S.; Pakalnis, Regina. Institute for the Study of Developmental Disabilities, 1640 West Roosevelt Road, Chicago, IL 60608 **Response to pentobarbital of pigmented vs albino C57BL/6J-c2J mice: a within-strain comparison of sleep times and lethal doses.** Behavioral and Neural Biology. 27(4):552-557, 1979.

A within strain comparison of the sleep times and lethal doses resulting from administration of pentobarbital to black vs. albino mice of the C57BL/6J inbred strain is presented. These coisogenic mice differed in one gene at the c-locus, but were otherwise genetically identical. Male pairs consisting of a black and a coisogenic albino littermate were injected weekly ip with sodium pentobarbital; dosage increased 10mg/kg per week. Median sleep times were consistently greater for albinos at dosages above 50mg/kg. Median sleep time differences increased with increasing dosage; there was a significant positive dosage/median sleep time difference correlation, and albinos' sleep times differed significantly from blacks' at 70, 100, 110, 120, 130, and 150mg/kg dosages. No black/albino differences in lethal dosages were found. It is reported that sleep time results extend, but lethal dose data contrast with, previous findings. 8 references. (Author abstract modified)

001911 Wetzel, W.; Getsova, V. M.; Jork, R.; Matthies, H. Institute of Pharmacology and Toxicology, Medical Academy, DDR-301 Magdeburg, Germany **Effect of serotonin on Y-maze retention and hippocampal protein synthesis in rats.** Pharmacology Biochemistry and Behavior. 12(2):319-322, 1980.

The effect of serotonin (5-HT) on consolidation of a brightness discrimination reaction was investigated in rats. A dose of 5mcg 5-HT, injected intrahippocampally immediately after training, impaired retention of the brightness discrimination tested 24 hours later. In biochemical experiments, leucine incorporation into hippocampal proteins in vivo was 32% inhibited

by 5mcg 5-HT. Leucine incorporation into proteins of hippocampal slices in vitro was decreased. The results seem to support Essman's assumption that inhibition of brain protein synthesis by 5-HT may be responsible for memory impairment but it is suggested that other possibilities for a mechanism of 5-HT amnesia should be discussed. 33 references. (Author abstract)

001912 Wiegant, Victor M.; Jolles, Jelle; Colbern, Deborah L.; Zimmermann, Emery; Gispén, Willem Hendrik. Division of Molecular Neurobiology, Institute of Molecular Biology, University of Utrecht, Padualaan 8, Utrecht, The Netherlands. **Intracerebroventricular ACTH activates the pituitary-adrenal system: dissociation from a behavioral response.** *Life Sciences*. 25(21):1791-1796, 1979.

Intracerebroventricular (i.c.v.) injection of synthetic adrenocorticotrophic hormone (ACTH1-24 and ACTH1-16) elevated plasma corticosterone levels and induced excessive grooming behavior in male Wistar rats. The grooming response could be elicited in hypophysectomized rats without concomitant elevation of plasma corticosterone. In intact rats, subcutaneous injection of ACTH1-24 (but not ACTH1-16) stimulated the release of adrenal corticosteroids without eliciting excessive grooming. In contrast to the reduced effectiveness of a second i.c.v. injection of ACTH in inducing the behavioral response, no single dose tolerance to the effect on the pituitary/adrenal system was observed. It is concluded that the effects of i.c.v. ACTH on plasma corticosterone levels and on behavior are mediated by two different central mechanisms. 27 references. (Author abstract modified)

001913 Wilcox, Richard E.; Smith, Robert V.; Anderson, Julie A.; Riffe, William H. Dept. of Pharmacology and Drug Dynamics Institute, College of Pharmacy, University of Texas, Austin, TX 78712. **Apomorphine-induced stereotypic cage climbing in mice as a model for studying changes in dopamine receptor sensitivity.** *Pharmacology Biochemistry and Behavior*. 12(1):29-33, 1980.

Apomorphine (APO) induced stereotypic cage climbing in mice was evaluated as a model for studying changes in dopamine receptor sensitivity following chronic administration of the potent butyrophenone neuroleptic spiroperidol. Spiroperidol induced a significantly enhanced response induced by APO (about a seven-fold increase) manifest by 48 hours (but not 24 hours) following cessation of the last chronic injection. Time response analyses demonstrated that the action of test doses of APO (1.0 or 4.5mg/kg, i.p.) was significantly prolonged in the chronic spiroperidol animals relative to controls. The supersensitivity in the spiroperidol treated animals lasted more than 3 weeks for each dose of the neuroleptic and the APO dose/response curve was shifted to the left in spiroperidol treated animals. Results are discussed in terms of the utility of the model for establishing dose response, time course, and duration of effect data within the same group of animals. 53 references. (Author abstract modified)

001914 Willow, Max; Carmody, John; Carroll, Peter. School of Physiology and Pharmacology, University of New South Wales, Kensington, New South Wales 2033, Australia. **The effects of swimming in mice on pain perception and sleeping time in response to hypnotic drugs.** *Life Sciences*. 26(3):219-224, 1980.

The effects of swimming-induced stress on pain perception and sleeping time in response to hypnotic drugs were studied in mice. Swimming stress was found to produce analgesia and to prolong pentobarbitone sleeping time. Both these effects were abolished by naloxone. Morphine in subanalgesic doses also prolonged pentobarbitone sleeping time in stressed mice. Neither swimming nor morphine had any effect on ethanol sleeping

time. This form of stress is considered to release an opioid (or opioids) within the brain with some specificity of interaction with other drugs. 9 references. (Author abstract modified)

001915 Winters, W. D.; Kott, Kayleen S. Dept. of Pharmacology, School of Medicine, University of California, Davis, CA 95616. **Continuum of sedation, activation and hypnosis or hallucinosis: a comparison of low dose effects of pentobarbital, diazepam or gamma-hydroxybutyrate in the cat.** *Neuropharmacology*. 18(11):877-884, 1979.

The effects of small doses of pentobarbital, diazepam, and gamma-hydroxybutyrate (GHB) were examined in freely moving cats with chronic cortical, subcortical, and nuchal muscle electrodes. All three drugs produced sedation at low doses and activation at slightly higher doses. At still higher doses, pentobarbital and diazepam induced hypnosis, but GHB induced hallucinosis. A dose/time continuum of sedation, activation, and hypnosis is suggested for hypnotic agents, and a continuum of sedation, activation, and hallucinosis for hallucinogenic agents. 14 references. (Author abstract modified)

001916 Wojcik, W. J.; Fornal, C.; Radulovacki, M. Dept. of Pharmacology, College of Medicine, University of Illinois at the Medical Center, Chicago, IL 60612. **Effect of tryptophan on sleep in the rat.** *Neuropharmacology*. 19(2):163-167, 1980.

The effects of tryptophan on sleep were investigated in rats implanted with EMG and EEG electrodes via analysis of EEG and EMG data for 6 hours following intraperitoneal injection of 30mg/kg or 120mg/kg of L-tryptophan. The smaller dose decreased the latency to the first slow wave sleep (SWS) episode by 15 minutes (43%) and to the first REM sleep episode by 18 min (27%). There were no changes in wakefulness, SWS, or REM sleep during the 6 hours of EEG recording. In contrast, the 120mg/kg dose did not affect sleep latencies but increased wakefulness and decreased REM sleep during the second hour of EEG recording. The reduction of SWS latency produced by the lower dose occurred at a time when the level of 5-hydroxyindoleacetic acid (5-HIAA) was elevated in the cortex and pons/medulla (i.e., 15 minutes postinjection). At the same time, hippocampal and cortical dopamine levels decreased while that of homovanillic acid did not change. The level of norepinephrine also decreased in the hippocampus. Whereas these changes in brain catecholamines were not observed 45 minutes after tryptophan administration, there was an elevation of 5-hydroxytryptamine in the pons/medulla and cortex as well as of 5-HIAA in the pons/medulla and hippocampus. The data suggest that the hypnotic effect of tryptophan may involve the normal sleep mechanism since similar neurochemical findings were reported during natural SWS. However, the effect may be limited to a certain dose range because a high dose produced waking rather than sleep. 28 references. (Author abstract modified)

001917 Wolfarth, S.; Coelle, E.-F.; Osborne, N. N.; Sontag, K.-H.; Wand, P. Institute of Pharmacology, Polish Academy of Sciences, 31-343 Krakow, Poland. **Drug-induced stereotypes and asymmetric behaviour after substantia nigra pars posterior (SNPP) lesions in cats.** *Brain Research*. 178(2-3):545-554, 1979.

Apomorphine and amphetamine-induced behavioral phenomena were studied in cats given 6-hydroxydopamine or electrothemic lesions of the posterior part of the substantia nigra (SNPP). Both drugs evoked stereotyped sniffing and head nodding in cats, but not the stereotyped gnawing and licking observed in rats similarly treated. Histological examinations revealed an inverse correlation between the dopamine specificity of the lesion and the degree of ipsilateral turning behavior. Results suggest that the ipsilateral asymmetric behavior induced by apomorphine and amphetamine was due to the destruction of a

noncatecholaminergic output. 31 references. (Author abstract modified)

001918 Wong, Roderick; Krantz, Leon; Krantz, Frances W. Dept. of Psychology, University of British Columbia, Vancouver, Canada V6T 1W5 **Effects of diphenylhydantoin on saline intake of rats, gerbils, and hamsters.** *Behavioral and Neural Biology*. 27(2):238-243, 1979.

Saline and water intakes were determined in rats, gerbils, and hamsters before and after i.p. injections of diphenylhydantoin (DPH, 4.0mg/100g) or vehicle. The DPH treated rats showed an increase in saline intake and preference relative to control rats only during the injection phase of the experiment. DPH did not alter saline intake in gerbils or hamsters. These findings are discussed in relation to the hypothesis that sodium appetite is enhanced through nonatriuretic drugs that stimulate sodium transport. 8 references. (Author abstract modified)

001919 Wong, Yu-wah; Chiu, Simon; Mishra, Ram K. Neuropharmacology Laboratory, McMaster University Medical Centre, Hamilton, Ontario L86 4J9, Canada **Effect of D-lysergic acid diethylamide on striatal choline acetyltransferase activity in the rat.** *Biochemical Pharmacology*. 28(14):2207-2209, 1979.

Striatal choline acetyltransferase (ChAT) activity and cataleptic response were determined in male Sprague-Dawley rats following subcutaneous injection of 50, 250, 375, or 500mcg/kg d-lysergic acid diethylamide (LSD). The lowest dose of LSD significantly increased striatal ChAT activity 2.5 hours after injection, but higher doses exerted no appreciable effect. In contrast, 50mcg/kg LSD failed to produce any appreciable degree of catalepsy, but the 375 and 500mcg/kg doses induced significant cataleptic reactions, with maximum effect 2.5 hours after injection. 24 references.

001920 Wood, Jeanette M. Dept. of Pharmacology, University of Otago Medical School, Dunedin, New Zealand **Effect of depletion of brain 5-hydroxytryptamine by 5,7-dihydroxytryptamine on ethanol tolerance and dependence in the rat.** *Psychopharmacology*. 67(1):67-72, 1980.

Brain 5-hydroxytryptamine (5-HT) was depleted in rats by intraventricular injection of 5,7-dihydroxytryptamine (5,7-DHT) prior to feeding rats a liquid diet containing ethanol, and the effects of depletion of 5-HT on ethanol tolerance and dependence were assessed. After withdrawal of ethanol, withdrawal reactions were significantly less severe in 5-HT depleted rats than control rats. Sleeping times after a standard dose of ethanol or pentobarbitone were significantly prolonged in 5-HT depleted rats. However, metabolic and pharmacodynamic tolerance developed to a similar extent in 5-HT depleted rats as in control rats. It is concluded that 5-hydroxytryptaminergic neurons are not directly involved in the development of physical dependence on or tolerance to ethanol. Depletion of brain 5-HT by 5,7-DHT appears to result in a nonspecific CNS depression that potentiates the depressant actions of ethanol and pentobarbitone and antagonizes the hyperexcitability of ethanol withdrawal. 31 references. (Author abstract modified)

001921 Woolf, Clifford J. Dept. of Physiology, Windeyer Building, Middlesex Hospital Medical School, Cleveland St., London W1P 6DB, England **Analgesia and hyperalgesia produced in the rat by intrathecal naloxone.** *Brain Research*. 189(2):593-597, 1980.

The effect of opiate receptor blockade in the spinal cord produced by intrathecal naloxone on the response to two different noxious stimuli was investigated in the rat. Intrathecal microinjections of saline, morphine, and naloxone were made into male Sprague-Dawley rats and the effects on the hot water tail im-

mersion test and on the electric shock vocalization test were determined. Intrathecal saline did not modify the rats' reaction to tail immersion in the hot water, but intrathecal naloxone at a dose of 7.5 mcg produced a small but significant prolongation of the response latency which was maximal 1 min postinjection and then declined slowly over 20 min. Higher doses of naloxone result in a dose dependent hyperalgesia. Although quantitatively different, the response to intrathecal naloxone in the electric shock vocalization test was similar, indicating that the effects of the naloxone are likely to be on afferent pathways. The hyperalgesic effects of naloxone at higher doses were consistent with the blockade of a tonic inhibition produced by the endogenous opioids in the spinal cord. It is suggested that the relatively high dose of naloxone required to produce the hyperalgesia may be related to the greater potency of naloxone in blocking a morphine binding with opiate receptors than in versing enkephalin binding. 15 references.

001922 Wu, Ming-Fung; Cruz-Morales, Sara E.; Quinan, Jay R.; Stapleton, June M.; Reid, Larry D. Rensselaer Polytechnic Institute, Troy, NY 12181 **Naloxone reduces fluid consumption: relationship of this effect to conditioned taste aversion and morphine dependence.** *Bulletin of the Psychonomic Society*. 14(5):323-325, 1979.

The correlation between the extent of conditioned taste aversion (CTA) under naloxone and the amount of sweetened morphine solution consumed voluntarily was tested. Ss were 40 naive male rats. No such correlation was found and no correlation was found between the CTA under naloxone and suppression of drinking under naloxone, suggesting that the reductions in drinking were unrelated to the illness producing effects indexed by the CTA test. In addition, naloxone suppression of drinking was unaffected by prior morphine administration with the administration of morphine given in a variety of ways, including dependence producing regimens of injections. It remains to be seen whether these findings have relevance for understanding processes of addiction or are a clue to endorphinergic functioning. 10 references. (Author abstract modified)

001923 Yamada, Katsushi; Furukawa, Tatsuo. Dept. of Pharmacology, School of Medicine, Fukuoka Univ., Fukuoka 814, Japan **Direct evidence for involvement of dopaminergic inhibition and cholinergic activation in yawning.** *Psychopharmacology*. 67(1):39-43, 1980.

The neurological mechanism involved in yawning in rats was investigated, and direct evidence for involvement of dopaminergic inhibition and cholinergic activation in yawning is discussed. Intraperitoneal injections of low doses of apomorphine, which preferentially activate presynaptic dopamine autoreceptors, elicited yawning. However, apomorphine, at a high dose of 2mg/kg, produced stereotypy which has been thought to be mediated by stimulation of postsynaptic dopamine receptors. The yawning and stereotypy did not occur simultaneously in the rat. The apomorphine-induced yawning was completely inhibited by pretreatment with fluphenazine or scopolamine, but markedly increased by reserpine, however it was not affected by methylscopolamine. Both physostigmine, an indirect acetylcholine agonist, and pilocarpine, a direct acetylcholine agonist, also induced yawning. This was abolished by scopolamine, and increased by reserpine. Fluphenazine did not affect the pilocarpine-induced yawning but increased the physostigmine-induced yawning. Results indicate that apomorphine elicits yawning by stimulating presynaptic dopamine receptors, and that dopaminergic inhibition and cholinergic activation are concomitantly involved in the yawning. 41 references. (Author abstract modified)

001924 Zolovick, Andrew J.; Avrih, Douglas; Jalowiec, John E. Dept. of Psychology, Bowling Green State University,

Bowling Green, OH 43402 **Reversible colchicine-induced disruption of amygdaloid function in sodium appetite.** *Brain Research Bulletin*. 5(1):35-39, 1980.

The functional role of the medial amygdaloid nuclei in the regulation of sodium appetite following acute sodium deficiency (hyponatremia and hypovolemia) was investigated via bilateral injections of the antimitotic drug colchicine into the medial amygdaloid nuclei. Colchicine resulted in a dissociation of the normally concurrent sodium appetite and water thirst in rats following formalin-induced hypovolemia and hyponatremia. While control rats drank the normally aversive sodium solution as well as water after formalin injection, colchicine treated animals failed to ingest the sodium solution but did consume the expected amount of water to compensate for hypovolemia. Sodium consumption, but not water consumption, remained significantly depressed in the colchicine treated rats when they were challenged again with formalin 11 days but not 20 days after amygdaloid injections. The latter results suggested complete recovery from the colchicine-induced amygdaloid dysfunction. It is concluded that colchicine may serve as a potentially useful technique for producing reversible lesions of known duration for the assessment of brain-behavior relationships. 52 references. (Author abstract modified)

001925 Zump, Doris; Michael, Richard P. Department of Psychiatry, Emory University School of Medicine, Atlanta, GA 30322 **Relation between the hormonal status of the female and direct and redirected aggression by male rhesus monkeys (Macaca mulatta).** *Hormones and Behavior*. 12(3):269-279, 1979.

The relationship between direct and redirected aggression by male rhesus monkeys and sexual activity was studied. Each of 16 feral reared male rhesus monkeys was paired with an ovariectomized female during daily 60 minute behavior tests. Each male received eight consecutive tests with an untreated female, eight tests when the female received injections of estradiol, and eight tests after estrogen was withdrawn. Of the 16 males, 11 threatened sufficiently often for numerical analysis (aggressive males). Two of these males showed no changes either in sexual activity or in agonistic behavior when the females were estrogenized. In the remaining nine males, there was increased sexual activity when the females were estrogenized and this was associated with a significant decrease in direct aggression and an increase in redirected aggression. The demonstration in the same males of an inverse relation between threats directed toward and away from the female supports the hypothesis that threats directed away from the sexual partner represent aggression aroused by the partner that is redirected onto the environment when sexual interest increases. 37 references. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

001926 Angevine, L. S.; Mehendale, H. M. Dept. of Pharmacology and Toxicology, University of Mississippi Medical Center, Jackson, MS 39216 **Chlorpheniramine uptake by isolated perfused rabbit lung.** *Toxicology and Applied Pharmacology*. 52(2):336-346, 1980.

The uptake and accumulation processes of labeled chlorpheniramine (CP), a phenylethanamine type of anorexigenic agent, were examined in artificially ventilated, recirculating, isolated perfused rabbit lung preparations. Perfusate and lung homogenate samples were analyzed for the parent compound and possible metabolites. No metabolism of CP was observed. Steady-state uptake was reached after 25 min perfusion. Higher pulmonary extraction of CP was observed from artificial medium than from whole blood. Lung uptake was concentration dependent and was saturable at a concentration of 1mM. Higher con-

centrations resulted in edematous and deteriorating preparations. Total CP uptake could be represented by a combination of non-linear saturable and a linear nonsaturable processes. Experiments with partial or complete depletion of Na, inclusion of harmaline or ouabain, inhibitors of Na dependent processes, suggested that CP uptake is partially Na dependent. In vitro lung slice experiments with Na free medium and medium containing harmaline or iodoacetate yielded similar results. Preloading the lung with an equivalent concentration of imipramine resulted in partial inhibition of CP uptake. However, CP preloading was without effect on imipramine uptake. 31 references. (Author abstract modified)

001927 Boeck, Vita; Jorgensen, Aksel. Research Laboratories, H. Lundbeck & Co. A/S, Ottilavej 7-9, DK-2500 Valby, Denmark **Electrocardiographic and cardiovascular changes in cats and dogs caused by high doses of amitriptyline given as conventional tablets or a sustained release preparation.** *Acta Pharmacologica et Toxicologica*. 46(3):161-170, 1980.

Electrocardiographic and hemodynamic changes in anesthetized cats and conscious dogs were compared following high doses of amitriptyline given as conventional tablets or as a sustained release preparation. Plasma or serum levels of amitriptyline and nortriptyline were also determined. Results show that the sustained release preparation had fewer toxic effects than the conventional tablets. Absorption was much slower after administration of the sustained release preparation than after the tablet administration, and lower amounts of the drug were absorbed from the sustained release preparation than from the tablets. 25 references. (Author abstract modified)

001928 Bornschein, Robert L.; Hastings, Lloyd; Manson, Jeanne M. Dept. of Environmental Health, University of Cincinnati, Cincinnati, OH 45267 **Behavioral toxicity in the offspring of rats following maternal exposure to dichloromethane.** *Toxicology and Applied Pharmacology*. 52(1):29-37, 1980.

Rats, divided into four treatment groups, were exposed to dichloromethane (DCM) or filtered air before and/or during gestation to assess the occurrence and extent of toxic effects on developing offspring. Progeny of dams exposed to DCM either before and/or during gestation exhibited altered rates of behavioral habituation to novel environments. No simple relationship between exposure period and behavioral outcome was observed: each of the treatment groups showed effects as a function of age at testing and behavioral task used. Treatment effects were detectable as early as 10 days old and were still demonstrable at 150 days old. Treatment effects were observed in both sexes in preweaning tests but were not observed in adult females. No effects of subacute DCM exposure were evident in growth rate, long-term food and water consumption, wheel running, or avoidance learning. Effects on habituation cannot be definitely attributed to a direct effect of DCM since elevated maternal COHb or DCM-induced changes in maternal/litter interactions could have been contributing factors. 13 references. (Author abstract modified)

001929 Culver, Bruce; Vernadakis, Antonia. Vernadakis, Dept. of Psychiatry, University of Colorado Medical Center, Denver, CO 80262 **Effects of anticonvulsant drugs on chick embryonic neurons and glia in cell culture.** *Developmental Neuroscience*. 2(2):74-85, 1979.

The responses of neurons and glial cells to diphenylhydantoin (DPH), 5-(p-hydroxyphenyl)-5-phenylhydantoin (HPPH), and phenobarbital were studied in cell cultures of dissociated chick embryo brain. Histological evaluations revealed fewer cell aggregates, fewer neurons, and less prominent neuronal processes in the DPH treated cultures than in control cultures. Cultures

treated with HPPH exhibited toxicity similar to those treated with DPH, but phenobarbital treated cultures did not differ significantly from control cultures. The incorporation of (14C)-leucine into protein was decreased in cultures treated with DPH, but not in those treated with phenobarbital. 34 references. (Author abstract modified)

001930 Dalterio, Susan L. Dept. of Obstetrics and Gynecology, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78284 **Perinatal or adult exposure to cannabinoids alters male reproductive functions in mice.** *Pharmacology Biochemistry and Behavior*. 12(1):143-153, 1980.

The effects of perinatal or adult exposure to cannabinoids on male reproductive functions in mice were investigated. Oral administration of delta-9-tetrahydrocannabinol (THC) or cannabinal (CBN) at a dose of 50mg/kg to pregnant and lactating female mice results in long-term effects on their male offspring, including: body weight regulation, pituitary/gonadal function, responsiveness to exteroceptive stimuli from conspecifics, and copulatory activity. Effects of perinatal exposure to cannabinoids on the male reproductive system did not become evident until after weaning (21 days of age). The effects of THC and CBN on male reproductive activities and function are compared. Results indicate that both psychoactive and nonpsychoactive constituents of marijuana affect pituitary/gonadal function in adult mice, and that the development of the male reproductive system is significantly altered in animals exposed to cannabinoids during critical periods of sexual differentiation. Moreover, some of the observed effects on male reproductive function and androgen dependent behaviors may be secondary to alterations in the endocrine system produced by nonpsychoactive and psychoactive components of marijuana. 86 references. (Author abstract modified)

001931 Fuller, Ray W.; Meyers, Donald B.; Gibson, William R.; Snoddy, Harold D. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Depletion of brain serotonin by chronic administration of p-chloroamphetamine orally to rats and dogs.** *Toxicology and Applied Pharmacology*. 48(3):369-374, 1979.

In Wistar rats, p-chloroamphetamine (PCA) lowered brain serotonin almost as effectively after a single oral dose as after i.p. injection. PCA also depleted brain serotonin when mixed with the diet, but the amount of food intake was reduced due to the anorectic action of PCA. When rats were fed diets containing PCA for 125 days, the degree of brain serotonin and 5-hydroxyindoleacetic acid depletion was maximal at 1 to 4 weeks and diminished with further drug ingestion. In rats fed diets containing PCA for 90 days, brain serotonin was slightly but significantly reduced 2 weeks after drug administration was stopped. Brain serotonin concentration was decreased in dogs at the end of 90 days of oral drug administration and did not return to control values within 2 weeks of drug termination. Results suggest that long lasting, neurotoxic damage to brain serotonin neurons is less likely when PCA is given orally than when it is injected i.p. 24 references. (Author abstract modified)

001932 Grudzinska, E.; Gidynska, T.; Rump, S. Miliatry Institute of Hygiene and Epidemiology, 01-163 Warsaw, Poland **Therapeutic value of anticonvulsant drugs in poisonings with an organophosphate.** *Archives Internationales de Pharmacodynamie et de Therapie*. 238(2):344-350, 1979.

The therapeutic effects of phenytoin, pentobarbital, diazepam, trimethadione, and phenoximide as adjuvants to atropine and obidoxime were examined in fluostigmine intoxicated female Wistar rats. Only trimethadione significantly elevated the median lethal dose for fluostigmine in rats treated with atropine

and obidoxime. None of the anticonvulsants completely protected against the lethal effects of the organophosphate. 11 references. (Author abstract modified)

001933 Hatoum, Nabil S.; Davis, W. Marvin. Dept. of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Morphine lethality in rats: effects of various central receptor blocking agents.** *Research Communications in Chemical Pathology and Pharmacology*. 24(2):251-257, 1979.

Interactions between morphine and commonly used receptor blocking agents were studied in female Sprague-Dawley rats. A lethal potentiation was observed between sublethal doses of morphine and the beta-adrenergic blocker propranolol. The alpha-adrenergic blocker phentolamine showed a lesser but significant potentiation of morphine, as did a moderate dose of atropine. No synergism was noted between morphine and methylatropine, haloperidol, or methysergide. Phentolamine and atropine, at a dose that did not synergize with morphine, both added significantly to the lethality of the combination of morphine and propranolol; methylatropine, haloperidol, and methysergide had no synergistic or antagonistic effects on the lethality of the drug combination. 13 references. (Author abstract modified)

001934 Ho, I. K.; Loh, H. H.; Way, E. Leong. Department of Pharmacology and Toxicology, University of Mississippi Medical Center, Jackson, MS 39216 **Toxic interaction between choline and morphine.** *Toxicology and Applied Pharmacology*. 51(2):203-208, 1979.

A systematic assessment of the acute toxicity induced by varying dosage combinations of choline and morphine was studied in both mice and rats. The studies reveal that the toxic interaction between morphine and choline treatment was time dependent and that the LD50 of each compound was markedly decreased by the coadministration of increasing doses of the other compound. The mortality to a combined fixed dose of morphine and choline was reduced by naloxone but not by physostigmine and atropine. The narcotic/choline interaction was stereospecific. In comparing two pairs of opiate enantiomers, only the active l-methadone and levorphanol exhibited a potentiating effect on toxicity, whereas the inactive d-methadone and dextrorphan did not. Results indicate that a potent interaction exists between opiates and choline; although the precise mechanism of the interaction is not clear, it appears to be more directly related to choline than to the opiates. 13 references. (Author abstract)

001935 Lipton, J. M.; Whisenant, J. D.; Gean, J. T. Dept. of Physiology, University of Texas Health Science Center, Dallas, TX 75235 **Hypothermia produced by peripheral and central injections of chlorpromazine in aged rabbits.** *Brain Research Bulletin*. 4(5):631-634, 1979.

The hypothermia produced by i.v. injection of 0.5 to 2.0mg/kg chlorpromazine (CPZ) in a thermoneutral environment was greater in New Zealand rabbits 2 to 4.5 years old than in those less than 24 months old. Intracerebroventricular (i.c.v.) administration of 1mcg CPZ produced greater hypothermia in older animals in thermoneutral environments, but 0.25 and 0.5mcg i.c.v. doses did not. The hypothermic effects of all three i.c.v. doses were enhanced in older rabbits exposed to cold. These findings suggest that this widely used tranquilizer may contribute to accidental hypothermia in geriatric patients. 23 references. (Author abstract modified)

001936 Lovell, K. L.; Jones, M. Z. Pathology Dept., Michigan State University, East Lansing, MI 48824 **Kainic acid neurotoxicity in the mouse cerebellum.** *Brain Research*. 186(1):245-249, 1980.

The neurotoxic effects of kainic acid (KA) in the mouse cerebellum following intracerebellar injection were studied. The lesions produced by 0.8mcg KA could be divided into three zones with indistinct borders: 1) the most severe damage was seen near the injection site, and was characterized by destruction of all neuronal cell types; 2) adjacent to this central zone was a region characterized by degeneration of all basket and stellate cells in the molecular layer, necrosis of varying numbers of granule cells, and sparing of most Purkinje cells; and 3) in the most peripheral zone, all granule and Purkinje cells were spared, while basket and stellate cells were destroyed. The results suggest that KA-induced destruction of cerebellar neurons is not directly related to extent of glutamatergic innervation. Findings are compared with those of other studies. 16 references.

001937 Muller, Jörn; Schulze, Svend. Dept. of Pharmacology, University of Copenhagen, 20 Juliane Mariesvej, DK-2100 Copenhagen O, Denmark **Imipramine cardiotoxicity: an electrocardiographic and haemodynamic study in rabbits.** *Acta Pharmacologica et Toxicologica.* 46(3):191-199, 1980.

Electrocardiographic and hemodynamic changes were observed in rabbits during continuous i.v. infusion of imipramine. Results show that the decrease in heart rate and change in heart rhythm induced by the tricyclic antidepressant were always preceded by a fall in arterial blood pressure and cardiac contractility. These findings suggest that a direct depressant action on the myocardium is involved in the cardiotoxic effects of imipramine, although a depressant effect on cardiac conduction, an anticholinergic effect, and altered adrenergic activity may also contribute. 28 references. (Author abstract modified)

001938 Myers, Robert R.; Shapiro, Harvey M. Department of Anesthesiology, Veterans Administration Hospital, San Diego, CA 92161 **Local cerebral metabolism during enflurane anesthesia: identification of epileptogenic foci.** *Electroencephalography and Clinical Neurophysiology.* 47(2):153-162, 1979.

Electrocorticographic activity was contrasted with local cerebral glucose uptake ((14C)2-deoxyglucose autoradiography) in 23 brain structures in order to identify the epileptogenic foci. Autoradiograms were obtained from sectioned rat brain following a 30 min period of steady-state anesthesia at 1, 1.5, or 2 minimum alveolar concentration (MAC) enflurane. Results indicate that the low seizure threshold hippocampus and related structures associated with the limbic system and its pathways are the epileptogenic foci for seizures induced with enflurane in the rat. At 1.5 MAC, it is reported, epileptiform activity spreads throughout the visceral brain when seizure threshold is at a minimum. 28 references. (Author abstract modified)

001939 Natelson, Benjamin H.; Hoffman, Scott L.; Cagin, Norman A. Dept. of Neurosciences, New Jersey Medical School, East Orange, NJ 07018 **A role for environmental factors in the production of digitalis toxicity.** *Pharmacology Biochemistry and Behavior.* 12(2):235-237, 1980.

The effects of changes in external milieu on the lethality of ouabain was studied. Guinea pigs experiencing restraint stress for the first time showed a greater susceptibility to the lethal effects of ouabain than nonstressed controls. Adaptation to the restraint procedure abolished this sensitization. This effect related to repeated experience with restraint and not to repeated human handling because repeatedly handled guinea pigs still showed sensitization to the lethal effect of ouabain when restrained for the first time. These data indicate that environmental factors will have to be considered in addition to changes in the internal milieu when trying to explain individual differences in sensitiv-

ity to toxicity while taking constant doses of digitalis. 10 references. (Author abstract)

001940 Nielsen-Kudsk, F.; Quist, Søren. Institute of Pharmacology, University of Aarhus, DK-8000 Aarhus C, Denmark **Myocardial pharmacokinetics of amitriptyline and clomipramine in the isolated, perfused rabbit heart.** *Acta Pharmacologica et Toxicologica.* 46(3):213-218, 1980.

The myocardial pharmacokinetics of amitriptyline and clomipramine were investigated in isolated rabbit hearts. Results reveal two compartment myocardial characteristics for amitriptyline and one compartment myocardial characteristics for clomipramine. The biological half-life of amitriptyline in the myocardium was about 37.7 minutes, and a pronounced cardiac accumulation of about 340mcg of the compound at steady state was observed. The myocardial half-life of clomipramine was about 106 minutes, and the accumulation at steady state was about 1055mcg. 25 references. (Author abstract modified)

001941 Olesen, Ole Vendelin; Thomsen, Klaus. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, DK-8240 Risskov, Denmark **Potassium-induced renal loss of sodium in lithium-treated rats.** *Acta Pharmacologica et Toxicologica.* 46(3):178-184, 1980.

The effects of dietary potassium on lithium-induced renal water and sodium losses were examined in male Wistar rats. Potassium did not significantly alter water intake in the lithium treated rats, but did cause a temporary increase in intake of sodium chloride, associated with renal loss of sodium. When animals were not allowed to replace the lost sodium by drinking more sodium chloride solution, plasma renin rose and body weight, lithium clearance, and water intake fell. It is concluded that high potassium intake could not cure the lithium-induced sodium and water-losing conditions and that prolonged lithium administration interfered with the mechanism for selective renal excretion of potassium. 15 references. (Author abstract modified)

001942 Olesen, Ole Vendelin; Thomsen, Klaus. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, DK-8240 Risskov, Denmark **Renal response to potassium infusion in rats given lithium for prolonged time.** *Acta Pharmacologica et Toxicologica.* 46(3):185-190, 1980.

In male Wistar rats given lithium in food for 3 weeks, infusion of potassium resulted in increased renal sodium, water, and lithium excretion. Sodium excretion and urine flow showed a positive linear correlation to potassium excretion, but the effects of potassium on sodium excretion and urine flow were 8 and 13 times higher, respectively, in the lithium treated rats than in controls. The concentration of sodium and potassium in the urine and the clearance of inulin were not significantly altered by potassium infusion. Lithium clearance and fractional excretion rose significantly during potassium infusion. 7 references. (Author abstract modified)

001943 Paulson, Ruta B.; Paulson, George W.; Jreisat, Salim. College of Dentistry, Ohio State University, 305 W. 12th Ave., Columbus, OH 43210 **Phenytoin and carbamazepine in production of cleft palates in mice: comparison of teratogenic effects.** *Archives of Neurology.* 36(13):832-836, 1979.

The teratogenic activity of two anticonvulsant drugs, phenytoin sodium and carbamazepine, was studied in pregnant mice who were fed the two drugs during days 8 to 13. Incidence of palatal defects and other abnormalities correlated with increasing dosages and blood levels of the drugs. Phenytoin produced a much higher incidence of teratogenic effects than carbamazepine. 18 references. (Author abstract modified)

001944 Rosenkrantz, Harris; Hayden, David W. EG&G Mason Research Institute, Worcester, MA 01608 **Acute and subacute inhalation toxicity of Turkish marihuana, cannabichromene, and cannabidiol in rats.** Toxicology and Applied Pharmacology. 48(3):375-386, 1979.

Fischer rats were exposed to a single daily dose of smoke from Turkish marihuana containing 1.2% cannabidiol (CBD) and cannabichromene (CBCH) and 0.25% delta-9-tetrahydrocannabinol (THC) or smoke from placebo marihuana impregnated with 0.6% CBD or CBCH 5 days a week for 17 to 25 days. An automatic inhaler presented cannabinoid doses of 1, 1.5, and 2mg/kg from Turkish marihuana or 0.6, 0.8, and 1.2mg/kg from CBD or CBCH marihuana. A 50% delayed toxicity occurred in both sexes at the high dose of Turkish marihuana, with no deaths in the CBD, CBCH, or placebo groups. Turkish marihuana smoke suppressed growth rates and respiration rates more than smoke containing CBD or CBCH with THC. Hematological variations were more closely associated with CBCH, but organ weight changes were more common with Turkish marihuana and CBD. The only histopathological finding was seminiferous tubule degeneration with interference in sperm maturation; this dose-related effect was most severe in CBD treated rats. Estimated median lethal dose values, based on cannabinoid content, were 10mg/kg for Turkish marihuana smoke and 35mg/kg for smoke containing CBD or CBCH. 43 references. (Author abstract modified)

001945 Salhab, Abdulazim S.; Yasuhara, Hajime; Dujovne, Carlos A. Clinical Pharmacology-Toxicology Center, University of Kansas Medical Center, Kansas City, KS 66103 **Surface activity, cellular uptake and cytotoxicity of tricyclic psychoactive drugs in vitro.** Biochemical Pharmacology. 28(11):1713-1718, 1979.

Isolated male Sprague-Dawley rat hepatocytes and Chang liver cell cultures were used to study the relationship between the magnitude of uptake by cells and the cytotoxic effects of the tricyclic antidepressant drugs amitriptyline (AT), imipramine (IM), and chlorpromazine (CPZ). Cell injury was evaluated by the extent of leakage of cytoplasmic and lysosomal enzymes from cells to the surrounding medium and by cytopathic changes seen under surface scanning electron microscopy after drug exposure. CPZ, AT, and IM showed decreasing rank order for both toxicity and uptake into cells. At equimolar concentrations in the medium, the uptake of CPZ by rat hepatocytes or Chang cells was 5 or 10 times greater than that of AT or IM. The rank order of surface excess of the drugs was also correlated with the rank order of uptake, suggesting that surface active properties may play a role in differences in bioavailability and toxicity of these drugs to liver cell membranes. 27 references. (Author abstract modified)

001946 Savolainen, H.; Helojoki, M.; Tengen-Junnila, M. Dept. of Industrial Hygiene and Toxicology, Institute of Occupational Health, Haartmaninkatu 1, SF-00290 Helsinki 29, Finland **Behavioural and glial cell effects of inhalation exposure to styrene vapour with special reference to interactions of simultaneous peroral ethanol intake.** Acta Pharmacologica et Toxicologica. 46(1):51-56, 1980.

Male Wistar rats exposed to 300ppm styrene vapour with simultaneous ethanol ingestion showed increased preening time after 4 weeks exposure and increased ambulation and rearing after 13 weeks exposure. Ethanol modified the accumulation of the solvent burden by delaying the peak solvent concentration in the perirenal fat to the eighth week of exposure. The styrene exposure had almost no effect on cerebral glial cells, but ethanol increased protein destruction; coexposure to ethanol and styrene decreased the magnitude of protein destruction in the glial cells.

The styrene effects had largely disappeared within 2 weeks of withdrawal, but brain RNA was lower than control levels after 2 weeks of ethanol deprivation. 25 references. (Author abstract modified)

001947 Siddik, Zahid H.; Barnes, Roger D.; Dring, L. Graham; Smith, Robert L.; Williams, R. Tecwyn. Laboratory of Toxicology, National Cancer Institute, NIH, Bethesda, MD 20205 **The metabolism of lysergic acid di(14C)ethylamide ((14C)LSD) in the isolated perfused rat liver.** Biochemical Pharmacology. 28(20):3081-3091, 1979.

Isolated female Wistar rat livers were perfused with radiolabeled lysergic acid diethylamide (LSD) and (D)-tartaric acid. After 4.5 hours, 44% of the added radioactivity was found in bile, 20% in the perfusate, and 20% in the liver itself. The radioactive compounds in the bile were identified as 14-hydroxy-LSD-glucuronide (21% of the added 14C), 13-hydroxy-LSD glucuronide (8%), 2-oxo-LSD (7%), and unchanged LSD (1%). Those in the pooled perfusate and homogenized liver were unchanged LSD (18%), 2-oxo-LSD (5%), a naphthostyryl derivative of LSD (4%), nor-LSD (4%), hydroxy-LSD glucuronides (3%), and de-ethyl-LSD (2%). 43 references. (Author abstract modified)

001948 Siddik, Zahid H.; Drew, Roger; Gram, Theodore E. Laboratory of Toxicology, National Cancer Institute, NIH, Bethesda, MD 20205 **The effect of chlorpromazine on the uptake and efflux of paraquat in rat lung slices.** Toxicology and Applied Pharmacology. 50(3):443-450, 1979.

Chlorpromazine inhibited the uptake and enhanced the efflux of paraquat in male Sprague-Dawley rat lung slices in a time and concentration dependent fashion. These *in vitro* findings suggested that chlorpromazine might be useful *in vivo* in reducing pulmonary paraquat content and pneumotoxicity. However, chlorpromazine potentiated the lethal toxicity of paraquat in the *in vivo* tests. This potentiation was correlated with a reduction in the urinary excretion of paraquat and an increase in pulmonary paraquat concentrations. 2 references. (Author abstract modified)

001949 Tank, A. William; Weiner, Henry. Dept. of Biochemistry, Purdue University, West Lafayette, IN 47907 **Ethanol-induced alteration of dopamine metabolism in rat liver.** Biochemical Pharmacology. 28(20):3139-3147, 1979.

The mechanism underlying ethanol-induced changes in dopamine metabolism were investigated in Wistar rat liver slices. Following incubation with labeled dopamine the ratio of 3,4-dihydroxyphenylacetic acid was about 10 in the absence of ethanol, but changed to about 0.25 in the presence of ethanol. This change in metabolism could not be attributed to the decreased liver cytosol NAD/NADH ratio or to the preferential oxidation of acetaldehyde over 3,4-dihydroxyphenyl acetaldehyde. Addition of alcohol dehydrogenase inhibitors prevented the ethanol-induced alteration in dopamine metabolism. 42 references. (Author abstract modified)

001950 Wedeen, Richard P.; Mailman, Richard B.; Breese, George R.; Krigan, Martin R.; Mushak, Paul; Mueller, Robert A. Veterans Administration Hospital, East Orange, NJ 07019 **Lead enhancement of lithium-induced polydipsia.** Science. 205(4407):725-726, 1979.

Methodological considerations and implications of the study by Mailman et al. concerning the hypothesized lead enhancement of lithium-induced polydipsia are discussed by Wedeen and Mailman et al. Wedeen contends that the published report of the research supporting the hypothesized neural mechanism of polydipsia is unclear due to the failure of the study to rule of

the direct renal effects of lead. Mailman et al. dispute that they administered massive doses of lead, and present data concerning lead absorption. Data which demonstrate that no alternation occurred in kidney function that would directly explain the increased lithium-induced polydipsia, are presented. It is reaffirmed that there may be permanent neural changes induced by postnatal exposure to lead. 7 references.

001951 Welch, J. J.; Kim, Heh Soon; Liebman, J. Research Dept., Pharmaceuticals Division, CIBA-GEIGY Corporation, Summit, NJ 07901 **Amphetamine-induced increases in dopaminergic single cell firing rate after haloperidol pretreatment. Correlation with extrapyramidal side effects.** *Neuropharmacology*. 19(4):371-377, 1980.

The effects of combined systemic treatment with d-amphetamine and haloperidol were investigated on firing rates in single dopamine cells within substantia nigra and ventral tegmentum, and the relationship between these effects and extrapyramidal side-effects of antipsychotic drugs is discussed. Joint administration of haloperidol and d-amphetamine increased firing rate of these neurons to levels exceeding those following treatment with haloperidol alone. This effect was observed regardless of which drug was administered first. No such enhancement of firing rate occurred when apomorphine was given in combination with haloperidol. It, therefore, seems possible that the increase in firing rate observed after d-amphetamine in combination with haloperidol is related to indirect feedback inhibition of these neurons rather than to activation of local regulatory mechanisms. The augmentation of the effect of haloperidol by d-amphetamine was not antagonized by BE-2254, an α -adrenergic receptor antagonist, nor by scopolamine. The d-amphetamine also increased firing rate following metoclopramide but not following thioridazine or clozapine. This unexpected interaction may, therefore, detect antipsychotics lacking extrapyramidal side-effects, and may provide insight into the mechanisms by which these side-effects are produced. 30 references. (Author abstract modified)

001952 Wright, Eugene E.; Bird, Janice L.; Feldman, Jerome M. Durham Veterans Administration Medical Center, Durham, NC 27710 **The effect of harmine and other monoamine oxidase inhibitors on N-acetyltransferase activity.** *Research Communications in Chemical Pathology and Pharmacology*. 24(2):259-272, 1979.

The monoamine oxidase inhibitors (MAOI) harmine and harmaline were potent inhibitors of N-acetyltransferase purified from golden hamster and Sprague-Dawley rat liver. However, other MAOI such as deprenyl, clorgyline, methysergide, cyproheptadine, phenelzine, pargyline, methyltryptamine, and tranylcypromine had slight or no effect on N-acetyltransferase. No correlation was found between the compounds' potencies in inhibiting MAO and N-acetyltransferase. 22 references. (Author abstract modified)

06 METHODS DEVELOPMENT

001953 Carmona, Euridice; Gomes, Cecilia; Trolin, Gustaf. Dept. Pharmacology, Escola Paulista de Medicina, C.P. 20372, 01000 Sao Paulo, S.P., Brazil **Purification of GABA on small columns of Dowex 50W; combination with a method for separation of biogenic amines.** *Acta Pharmacologica et Toxicologica*. 46(3):235-240, 1980.

Modifications of previous methods for separation of biogenic amines which permit separation of virtually pure GABA are described. GABA concentrations determined in various parts of rat brain by this method were of the same order of magnitude as those reported by other laboratories. The present method permits GABA and other substances of neuropharmacological in-

terest to be separated from the same tissue, using inexpensive equipment. 17 references. (Author abstract modified)

001954 Cowan, Alan; Geller, Ellen B.; Adler, Martin W. Department of Pharmacology, Temple University School of Medicine, Philadelphia, PA 19140 **Classification of opioids on the basis of change in seizure thresholds in rats.** *Science*. 206(4417):465-467, 1979.

Twenty opioids were subdivided into four classes by using flurothyl-induced seizures in rats to measure dose/response relationships, stereospecificity, naloxone sensitivity, and tolerance/cross-tolerance. Data supported current theories of multiple receptor types. Since the receptors involved mediated effects that were antagonized, enhanced, or unaffected by naloxone, the model is uniquely suitable for detecting novel narcotic antagonists that can be used to differentiate opiate receptors in other systems. 27 references. (Author abstract)

001955 Dames, W.; Joo, F.; Wolff, J. R. Max-Planck-Institut für biophysikalische Chemie, Abt. Neurobiologie, Neuroanatomie, Postfach 968, D-3400 Göttingen, Germany **A method for localized and long-lasting microapplication of drugs into nervous tissue of freely moving animals.** *Experimental Brain Research*. 36(2):259-264, 1979.

A method is described for localized microapplication of drugs into nervous tissue of freely moving rats. Fairly constant release of material was observed over a period of more than 3 weeks. The amount of substance released was small because the rate of release was determined largely by diffusion rather than by mass movement of solution. 12 references. (Author abstract)

001956 de Langen, Cees D. J.; Mulder, Arie H. Mulder, Dept. of Pharmacology, Free University Medical Faculty, Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands **Compartmental analysis of the accumulation of 3H-dopamine in synaptosomes from rat corpus striatum.** *Naunyn-Schmiedeberg's Archives of Pharmacology*. 308(1):31-39, 1979.

A method for quantifying the accumulation of radiolabeled dopamine (3H-DA) in striatal synaptosomes after superfusion with low concentrations of 3H-DA was developed. With synaptosomes from male Wistar rat striatum, extracellular 3H-DA disappeared from the superfusion chambers within 10 minutes, after which a steady state of efflux was rapidly established. Accumulated 3H-DA distributed in two compartments, an efflux compartment and a bound fraction that did not contribute to the efflux. Radioactivity extracted from synaptosomes superfused with 3H-DA consisted of about 90% unmetabolized DA, and this percentage increased slightly with time. Cocaine and tyramine (10mM) each inhibited the accumulation of 3H-DA by 85%. Uptake kinetic data indicated that at least 90% of the 3H-DA retained was transported by the high affinity membrane carrier for DA. The maximal rate of uptake was 100pmol/mg protein/minute. Data indicate that this method permits a reliable differentiation between the uptake inhibiting and releasing actions of drugs. 26 references. (Author abstract modified)

001957 Gooch, Charles F.; Rasband, Wayne S.; Sokoloff, Louis. Laboratory of Cerebral Metabolism, NIMH, Bethesda, MD 20205 **A computer assisted image processing system for the analysis of autoradiographs of cerebral metabolic activity.** *Bethesda, MD, NIMH*, 1979. 30 p.

A computerized image processing system has been developed for quantitative analysis of the autoradiographs obtained with the (14C)deoxyglucose method. By means of this system, these cerebral metabolic images can be digitized and the resultant data can be manipulated for image construction, enhancement, enlargement, and microdensity metric analysis. It is also possible

to generate quantitative color coded metabolic maps that display the distribution of the actual rates of local glucose utilization throughout the entire central nervous system in regions as small as 100 μm or less. 20 references. (Author abstract)

001958 Havey, D. C.; Caspary, D. M. Dept. of Pharmacology, Southern Illinois University School of Medicine, Springfield, IL 62708 **A simple technique for constructing multibarrel microelectrodes.** *Electroencephalography and Clinical Neurophysiology.* 48(2):249-251, 1980.

The construction of a multibarrel microelectrode for intracellular or extracellular recording and iontophoresis is described. A protruding glass recording micropipette is attached to a five barrel iontophoretic electrode. The piggy back microelectrode can be assembled in 10 to 15 minutes from readily available inexpensive materials. 6 references.

001959 Hazum, Eli; Chang, Kwen-Jen; Cuatrecasas, Pedro. Department of Molecular Biology, Wellcome Research Laboratories, Research Triangle Park, NC 27709 **Role of disulphide and sulphhydryl groups in clustering of enkephalin receptors in neuroblastoma cells.** *Nature.* 282(5739):626-628, 1979.

The effects of disulphide and sulphhydryl reagents on the clustering of opiate (enkephalin) receptors in N4TG1 neuroblastoma cells were examined. It is reported that in these cells there are reactive sulphhydryl and disulphide groups which are essential for cluster formation (but not binding), and that a sulphhydryl/disulphide exchange reaction may be involved in this process. In addition, the sulphhydryl reagents seem to dissociate the two steps of binding and cluster formation, and thus provide a tool for studying the pharmacological importance of receptor clustering. 16 references. (Author abstract modified)

001960 Katz, R. J.; Gormezano, Glen. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **A rapid and inexpensive technique for assessing the reinforcing effects of opiate drugs.** *Pharmacology Biochemistry and Behavior.* 11(2):231-233, 1979.

Adult male Sprague-Dawley rats were placed in an apparatus consisting of two distinctive interconnected chambers. Choice preferences developed and stabilized over three 30 min exposures. Central injection of morphine or an enkephalin analogue in conjunction with placement upon the nonpreferred side caused a preference shift which was not evident in control animals. Classical conditioning of opiate effects to distinctive environments may offer a novel means of assessing the hedonic effects of these compounds. 13 references. (Author abstract)

001961 Kudo, Yoshihisa; Nagai, Yasuo; Fukuda, Hideomi. Mit-subishi-Kasei Institute of Life Sciences, 11 Minamiooya, Machida-Shi, Tokyo 194, Japan **Decrease in the extracellular potassium activity of the frog spinal cord during the application of aliphatic anions.** *Brain Research.* 179(1):190-194, 1979.

Alterations of extracellular potassium activity of the frog spinal cord were examined during application of aliphatic anions frequently used substituted for chloride ions in pharmacological and physiological experiments. Extracellular potassium activity was significantly reduced by sodium acetate, sodium propionate, and sodium butyrate; during application of these anions, spontaneous activity in ventral and dorsal roots decreased considerably, and ventral and dorsal root potentials (measured by the sucrose gap method) were hyperpolarized. Sodium methylsulfate and sodium isethionate had no significant effect on extracellular potassium activity. Results indicate that the aliphatic anions have significant effects on the neuronal membrane and should not be considered inactive substitutes for the chloride ion. 14 references.

001962 Kvamme, E.; Olsen, B. E. Neurochemical Laboratory, Oslo University Psychiatric Clinic, Vinderen, Oslo 3, Norway **Substrate mediated regulation of phosphate-activated glutaminase in nervous tissue.** *Brain Research.* 181(1):228-233, 1980.

In Wistar rat brain synaptosome preparations, functionally significant phosphate activated glutaminase (PAG) activity was largely determined by substrate concentration. PAG activity was rapidly inhibited when glutamine concentration was high, but was maintained at a more steady level when the glutamine concentration was low. Results suggest that in vitro measurements of total PAG activity may not be significant if not correlated with the concentrations of glutamine available for the reaction. 29 references.

001963 Laties, Victor G. Department of Radiation Biology and Biophysics, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 **I. V. Zavadskii and the beginnings of behavioral pharmacology: an historical note and translation.** *Journal of the Experimental Analysis of Behavior.* 32(3):463-472, 1979.

An application of the method of conditioned reflexes to pharmacology is reported, as conducted by I. V. Zavadskii, a researcher in Pavlov's laboratory between 1907 and 1909. The study has many of the characteristics of modern behavioral pharmacology and involved investigation of the effects of alcohol, morphine, cocaine, and caffeine on the conditioned salivary reflex of dogs. A translation of the paper is presented, along with brief comments on his life. (Author abstract modified)

001964 MacKichan, J.; Duffner, P. K.; Cohen, M. E. State University of New York, Buffalo, NY 14222 **Adsorption of diazepam to plastic tubing.** *New England Journal of Medicine.* 301(6):332-333, 1979.

Studies indicating that diazepam, prescribed for convulsions, anxiety, and preoperative and postoperative anesthesia, is adsorbed by plastic tubing during continuous infusion are reported. Because of the various factors (diazepam concentration, flow rate, and tubing type) that can contribute to the unpredictability of the infusion system, it is recommended that intravenous administration be restricted to direct venous injections. It is also suggested that the practice of storing diazepam in plastic syringes should be discouraged. 4 references.

001965 Marini, James L.; Williams, Suzanne P.; Sheard, Michael H. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06508 **Simultaneous assay for L-tryptophan, serotonin, 5-hydroxyindoleacetic acid, norepinephrine and dopamine in brain.** *Pharmacology Biochemistry and Behavior.* 11(2):183-187, 1979.

A routine simultaneous assay for L-tryptophan, serotonin, 5-hydroxyindoleacetic acid, norepinephrine and dopamine is described which uses a cation exchange resin for separations and standard fluorometric methods for analyses. Practicability of the ion exchange chromatography is enhanced by means of a novel apparatus, and the procedure has the flexibility to permit extension to other endogenous compounds using published techniques. 13 references. (Author abstract)

001966 Melchor, Christine L.; Mueller, Allan; Deitrich, Richard A. Dept. of Pharmacology, University of Colorado Medical Center, Denver, CO 80262 **Half-lives of salsolinol and tetrahydropapaveroline hydrobromide following intracerebroventricular injection.** *Biochemical Pharmacology.* 29(4):657-658, 1980.

The half-lives of salsolinol and tetrahydropapaveroline hydrobromide (THP), amine aldehyde condensation products of alcohol, were determined following intracerebroventricular injection.

tion, as a preliminary step in the investigation of the physiological action of tetrahydroisoquinolines (TIQs). It is noted that the hypothesis that TIQs are formed following the ingestion of alcohol has not been tested due to the failure to detect the formation of these amine aldehyde condensation products after the administration of alcohol. Results indicate that doses below the level of detection (2ng/g) for the most sensitive assay which has yet been used to determine whether or not TIQs form after the ingestion of alcohol, are capable of altering behavior. 13 references.

001967 Mucha, R. F. Dept. of Pharmacology, University of Toronto, Toronto, Ontario, Canada M5S 2S1 **Indwelling catheter for infusions into subcutaneous tissue of freely-moving rats.** *Physiology & Behavior*. 24(3):425-428, 1980.

The use of a permanently implanted catheter, designed for drug administration to freely moving rats, was examined with male Wistar rats. The catheter, placed subcutaneously (SC) along the length of the rat's back, consisted of silicone tubing punched with tiny holes to allow a drug solution to pass. Analgesia produced in rats by morphine sulfate delivered through the catheter was comparable to that produced by SC hypodermic injection, but more rapid in onset. Sodium pentobarbital was absorbed by the blood significantly more rapidly following administration through the catheter than following hypodermic administration. 13 references. (Author abstract modified)

001968 Overton, Donald A. Temple University School of Medicine, Eastern Pennsylvania Psychiatric Institute, Philadelphia, PA 19129 **Drug discrimination training with progressively lowered doses.** *Science*. 205(4407):720-721, 1979.

Drug discrimination training with progressively lowered doses, wherein rats eventually learned to discriminate extremely low doses of phenobarbital, chlorthalidone, cyclazocine, and fentanyl, is described. During successive 10 day blocks of training sessions, all drug vs. no drug conditions were discriminated, and these discriminations were maintained during reductions in dosage ranging from 60% to 95% of initial dosages. Results indicate that drug discrimination procedures provide a test procedure that can be as sensitive as behavioral tests specifically developed to respond to the effects of individual classes of drugs. Implications for theoretical accounts of state-dependent learning and for psychoactive drug research methodology are discussed. 8 references. (Author abstract modified)

001969 Peralta, E.; Yang, H.-Y.T.; Hong, J.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Combination of enzymatic and mass fragmentographic assays for the identification and measurement of (met5)-enkephalin.** (Unpublished paper). Washington, DC, NIMH, 1979. 26 p.

A gas chromatography mass spectrometry (GC-MS) method, which can be used to quantify met5-enkephalin (ME) in brain but not in adrenal medulla, is described. Dipeptidyl-aminopeptidase-I (D.A.P.I.) was used to hydrolyze the penta-peptide ME into the dipeptides Tyr-Gly and Gly-Phe and methionine. The dipeptides could be derivatized and resolved by GC; quantification of these dipeptides was obtained by single ion monitoring. Tissue samples were prepurified and used as substrate for D.A.P.I. The yield of methionine and of the two dipeptides increases with time. Since the same dipeptides are produced by ME and leu5-enkephalin, the use of the ratios of the quantities of the two dipeptides with methionine could be used for recognition. Since the only internal standard available was one with deuterated methionine, the measurement of methionine released by D.A.P.I. from the prepurified tissue could be used to measure

ME content in tissues that contain a small amount of heterogeneity in the molecular forms of ME. 8 references.

001970 Petereson, J. E.; Graham, M.; Banks, W. F.; Benziger, D.; Rowe, E. A.; Clemans, S.; Edelson, J. Dept. of Drug Metabolism and Disposition, Sterling-Winthrop Research Institute, Rensselaer, NY 12144 **Plasma pentazocine radioimmunoassay.** *Journal of Pharmaceutical Sciences*. 68(5):626-628, 1979.

A sensitive and specific radioimmunoassay of dog and human plasma pentazocine is described. Rabbit antiserum and the second antibody method separated bound from free pentazocine. The radioimmunoassay employed a 125I-labeled radioligand and required extraction from the sample prior to quantitation. The method had a detection limit of about 200pg/assay tube (1ng/ml). The assay was used successfully to measure pentazocine in the plasma of beagle hounds given 0.3mg/kg i.v. pentazocine. The decline in plasma levels fitted a two compartment body model with a 100 minute mean overall half-life and a 3.2liter/hour mean plasma clearance rate. 18 references. (Author abstract)

001971 Po, A. Li Wan; Irwin, W. J. Irwin: Dept. of Pharmacy: University of Aston, Gosta Green, Birmingham B4 7ET, England **A high performance liquid chromatographic assay of cis- and trans- isomers of tricyclic neuroleptic drugs.** *Journal of Pharmacy and Pharmacology*. 31(8):512-516, 1979.

A high performance liquid chromatographic assay procedure is described which enables the separation, detection and quantification of the cis and trans isomers of tricyclic neuroleptic drugs. The method is applicable to the analysis of flupenthixol, clopenthixol, chlorprothixene, doxepin, and dothiepin. Measurement of the isomer ratios in various samples of flupenthixol indicated small batch to batch variations. The determination of the isomer ratio in formulation was shown to rely on the complete extraction of the medicament. This is due to the differential release of the components from the tablet matrix, with the cis isomer favored. Little difference was observed between the adsorption isotherms of the two components (onto charcoal). Clear implications for the pharmacokinetics of these drugs were found. 31 references. (Author abstract modified)

001972 Schechter, Martin D.; Chance, William T. Dept. of Pharmacology, Northeastern Ohio Universities College of Medicine, 4209 State Route 44, Rootstown, OH 44272 **Non-specificity of depression.** *European Journal of Pharmacology*. 60(2/3):139-142, 1979.

The effects of several drugs were tested in the behavioral despair model of depression, in which mice show a characteristic immobile posture following 2 to 3 minutes of forced swimming in a restricted space. Imipramine decreased the duration of immobility in a 4 minute swimming test in a dose related manner. However, immobility was also reduced by caffeine, triiodothyronine, and pentobarbital. Results indicate that the behavioral despair swimming test does not specifically identify drugs with antidepressant activity. 13 references. (Author abstract modified)

001973 Schoener, E. P.; Hager, P. J.; Felt, B. T.; Schneider, D. R. Dept. of Pharmacology, Wayne State University, School of Medicine, Detroit, MI 48201 **Cyclic nucleotides in the rat neostriatum: push-pull perfusion studies.** *Brain Research*. 179(1):111-119, 1979.

A push/pull perfusion technique was used to study cyclic AMP and cyclic GMP in vivo in the male Sprague-Dawley rat caudate nucleus. Addition of dopamine to the perfusion fluid elicited dose dependent increases in both cyclic AMP and cyclic GMP perfusate concentrations. Pretreatment with the dopamine

antagonist, pimozide, significantly depressed both nucleotide responses to dopamine perfusion over the dose range studied. Results are consistent with data obtained in *in vitro* studies using slices and homogenates of these areas. It is concluded that the push/pull perfusion technique is a useful means of studying extracellular cyclic nucleotide levels in a discrete brain region, *in vivo*, under dynamic conditions. 34 references. (Author abstract modified)

001974 Skomedal, T.; Grynne, B.; Osnes, J. B.; Sjetnan, A. E.; Oye, I. Institute of Pharmacology, University of Oslo, P. O. Box 1057, Blindern, Oslo 3, Norway **A radioimmunoassay for cyclic AMP (cAMP) obtained by acetylation of both unlabeled and labeled (3H-cAMP) ligand, or of unlabeled ligand only.** *Acta Pharmacologica et Toxicologica*. 46(3):200-204, 1980.

A sensitive radioimmunoassay for cyclic AMP, based on acetylation of both tritiated cyclic AMP and unlabeled ligand, is described. The limit of detection is 7fmol per tube. When only the unlabeled ligand is acetylated, increased sensitivity is obtained with no loss in specificity. 11 references. (Author abstract modified)

001975 Slater, P.; Longman, D. A. Physiology Dept., Medical School, University of Manchester, Manchester M13 9PT, England **Effects of diazepam and muscimol on GABA-mediated neurotransmission: interactions with inosine and nicotinamide.** *Life Sciences*. 25(23):1963-1967, 1979.

An *in vivo* method for detecting drugs with GABA mimetic properties was used to examine the effects of inosine, nicotinamide, and diazepam in the rat globus pallidus. Inosine and nicotinamide completely prevented the GABA mimetic action of diazepam but neither compound alone had any GABA-like activity. These findings suggest that inosine and nicotinamide are able to antagonize but are not able to mimic the GABA-like actions of diazepam at the benzodiazepine receptor. 17 references. (Author abstract modified)

001976 Sokoloff, Louis. Laboratory of Cerebral Metabolism, NIMH, Bethesda, MD 20205 **Mapping local cerebral functional activity by measurement of local cerebral glucose utilization with the (14C)deoxyglucose method. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 16 p.

A method that was developed to measure the rates of glucose utilization in the individual structural and functional components of the central nervous system is described. It can be applied to conscious as well as anesthetized animals. The method is based on the use of (14C)deoxyglucose as a tracer for glucose consumption. (14C)deoxyglucose-6-phosphate accumulates in the tissue in a mathematically definable relationship to the rate of the tissue's glucose utilization. The (14C)deoxyglucose-6-phosphate concentrations in the various tissues of the nervous system are measured by a quantitative autoradiographic technique. The autoradiographs themselves are pictorial representations of the relative rates of glucose consumption in these tissues. Application of this method to rats and monkeys in various physiological, pharmacological, and pathological states demonstrates a clear and close relationship between the local levels of functional activity and energy metabolism. The method appears to be useful for mapping functional neural pathways on the basis of evoked metabolic responses and for identifying loci of actions of pharmacological agents. 29 references. (Author abstract)

001977 Tappaz, Marcel L.; Pujol, Jean-Francois. Dept. de Medecine Experimentale, Groupe de Neurochimie Fonctionnelle, Université Claude Bernard, 8, Avenue Rockefeller, F-69008 Lyon, France **Estimation of the rate of tryptophan hydroxylation**

***in vivo*: a sensitive microassay in discrete rat brain nuclei.** *Journal of Neurochemistry*. 34(4):933-940, 1980.

The rate of tryptophan hydroxylation *in vivo* was estimated in discrete rat brain nuclei by measuring L-5-hydroxytryptophan (5-HTP) accumulated after pharmacological blockade of 5-HTP decarboxylase by NSD 1015, using a sensitive radioenzymatic microassay. This method is described. Effects of parachlorophenylalanine, chloral hydrate anaesthesia, and pargyline pretreatment on tryptophan hydroxylation are also described. As illustrated by these few pharmacological manipulations, this method allows the study of the regulation of tryptophan hydroxylation *in vivo* with an improved anatomical resolution. It is reported that investigations can be carried out in the various raphe nuclei and their corresponding terminals in discrete brain areas simultaneously. 28 references. (Author abstract modified)

001978 Vorhees, Charles V.; Butcher, Richard E.; Brunner, Robert L.; Sobotka, Thomas J. Dept. of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH 45229 **A developmental test battery for neurobehavioral toxicity in rats: a preliminary analysis using monosodium glutamate, calcium carrageenan, and hydroxyurea.** *Toxicology and Applied Pharmacology*. 50(2):267-282, 1979.

A test battery for evaluating developmental neurobehavioral toxicity was examined. Monosodium glutamate (MSG) and calcium carrageenan (CC) were used to obtain preliminary data with Sprague-Dawley rats using continuous dietary exposure from prior to conception through 90 days of postnatal life. Three dose levels were used with each of the food additives and data were compared to controls. Negative controls were fed normally and positive controls were exposed to hydroxyurea on the 12th day of gestation. Differences between MSG and negative control groups were observed in swimming development, open field, and active and passive avoidance testing. Effects observed in the CC groups were inconsistent and not dose related. It is suggested that the test protocol used in the research could serve as a usable screening technique for developmental neurobehavioral toxicity. 43 references. (Author abstract modified)

001979 Weiler, Molly H.; Misgeld, Ulrich; Bak, Il Jin; Jenden, Donald J. Dept. of Pharmacology, School of Medicine, University of California, Los Angeles, CA 90024 **Acetylcholine synthesis in rat neostriatal slices.** *Brain Research*. 176(2):401-406, 1979.

Acetylcholine (ACh) synthesis was studied in rat neostriatal slices in which the electrophysiological integrity of the cholinergic synapse was maintained for as long as 10 hours after slice preparation. The rate of ACh synthesis in these slices during the first 5 minutes of incubation (0.277nmol/mg protein/minute) was 1.3 to 10 times higher than most *in vivo* estimates of ACh turnover in this tissue. ACh levels in neostriatum, hippocampus, and frontal cortex were 4 to 10 times higher than those reported for the same brain areas after microwave fixation *in situ*. The possibility that *in vitro* values are artefactually high or that methods for measuring ACh levels *in vivo* are inadequate is discussed. 36 references.

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

001980 Baiotti, Gianni. Medical Department B, Molinette Hospital, Turin, Italy **Comparative trial of a new hypnotic (Finorgal) with nitrazepam and triclofos sodium.** *Journal of International Medical Research.* 7(5):383-386, 1979.

Thirty patients complaining of insomnia were studied in a double-blind trial with crossover of the new hypnotic Finorgal, nitrazepam, and triclofos sodium. Finorgal given as a hypnotic produced similar results to nitrazepam and triclofos sodium in terms of induction of sleep, duration, and quality of sleep, dream recall, and morning hangover. Reported side-effects were not serious and occurred less frequently in association with Finorgal treatment than with nitrazepam or triclofos sodium. Laboratory investigations gave no indication of the development of any drug toxicity during the 3 week period of the trial. 2 references. (Author abstract)

001981 Baiotti, Gianni. Medical Department B Molinette Hospital, Turin, Italy **Comparison of a new hypnotic (Finorgal) with placebo in a double-blind trial.** *Journal of International Medical Research.* 7(5):387-390, 1979.

The hypnotic effects of the new drug Finorgal (ethchlorvynol with diphenhydramine) were compared with those of placebo in a double-blind study with crossover of treatments in 35 hospital inpatients. During the 4 week period of Finorgal treatment, there was a significant reduction in the mean time elapsing between the administration of the hypnotic and the onset of sleep, and a significant increase in the duration of sleep, compared with the 4 weeks of placebo treatment. There was also a significant increase in the proportion of nights when the patients felt they had slept well, and in the incidence of morning hangover and nocturnal confusion during the Finorgal treatment periods. Patients had to be actively woken in the morning significantly more often following Finorgal administration. In patients experiencing pain in the night there was a significant reduction in the occurrence of pain during the nights when Finorgal had been given. 3 references. (Author abstract)

001982 Brown, D.; Scott, D. H. T.; Scott, D. B.; Meyer, M.; Westerlund, D.; Lundstrom, J. Lundstrom: Astra Lakemedel AB, Research and Development Laboratories, S-151 85 Sönderdal, Sweden **Pharmacokinetics of zimelidine: systemic availability of zimelidine and norzimelidine in human volunteers.** *European Journal of Clinical Pharmacology.* 17(2):111-116, 1980.

The systemic availability of a new antidepressant, zimelidine, and of its pharmacologically active metabolite, norzimelidine, was studied in six healthy male volunteers. Three single doses of zimelidine and two single doses of norzimelidine were given to each volunteer, allowing at least 7 days between administrations. Plasma concentrations of zimelidine and norzimelidine were determined in serial blood samples by HPLC. Following oral zimelidine peak plasma concentrations of the metabolite were attained about 3 hours after dosing. Oral administration of norzimelidine itself resulted in a plasma concentration profile for this compound that was similar to that observed after oral zimelidine. Using the plasma concentration data following intravenous infusion of each compound, the elimination half-lives for zimelidine and norzimelidine were calculated. The substantially longer elimination half-life of norzimelidine was apparently the result of a larger volume of distribution for this metabolite, as compared to zimelidine. The calculated bioavailability of zimelidine was 26% following a 25mg oral dose, an 29% after a 100mg dose. The bioavailability of norzimelidine was 66%. However,

oral administration of zimelidine resulted in as much or more norzimelidine itself. It is suggested that a large part of the activity of the drug may be due to the metabolite. 12 references. (Author abstract modified)

001983 Eadie, Mervyn J. Dept. of Medicine, Clinical Sciences Building, Royal Brisbane Hospital, Herston Road, Brisbane, Queensland 4029, Australia **Which anticonvulsant drug?** *Current Therapeutics.* 20(1):29-34, 36-37, 1979.

Elements of successful anticonvulsant therapy are discussed including selection of the appropriate drug and determination of appropriate dosage. A therapeutic guide flow chart is provided to assist physicians in the selection of anticonvulsant drugs. The aim of therapy is to completely control epilepsy for a sufficient period of time so that the epileptic tendency dies out, and the patient is cured of the disorder. This often requires several years of complete suppression.

001984 Fowler, L. K. Montedison Pharmaceuticals Limited, Kingmaker House, Barnet, Hertfordshire, England **Euhypnos Forte (temazepam) for resistant insomnia: post-marketing surveillance, an interim report.** *Journal of International Medical Research.* 7(5):379-382, 1979.

The performance of Euhypnos Forte, a new high-dose temazepam preparation, in the treatment of insomniac patients resistant to conventional hypnotic dosage was monitored by post-marketing surveillance. The analysis includes 2,043 first reports of 2 weeks treatment and 669 second reports of 3 months treatment. More than 95% of the patients took a nightly dose of two capsules, temazepam 40mg. Adverse reactions were generally acceptable, consisting mainly of headache, vivid dreams, gastrointestinal disturbances, and hangover effects. The preparation was effective in 88.6% of patients at 2 weeks and 95.8% at 3 months. All patients had previously found other hypnotics ineffective. Euhypnos Forte was rated effective by 85.5% of the 874 patients who had previously found nitrazepam unsatisfactory, and by 90.0% of the 201 who found barbiturates unsatisfactory. 3 references. (Author abstract modified)

001985 Gillin, J. Christian; Sitaram, N.; Duncan, Wallace C. National Institute of Mental Health, Building 10, Room 3N224, 9000 Rockville Pike, Bethesda, MD 20205 **Muscarinic supersensitivity: a possible model for the sleep disturbance of primary depression?** *Psychiatry Research.* 1(1):17-22, 1979.

Data from a study (Sitaram et al., 1979) which suggested that supersensitivity developed in normal volunteers who received scopolamine for 3 consecutive mornings are analyzed. The sleep changes resemble many of the abnormalities observed in the sleep of patients with primary depression: increased sleep latency and reduced REM latency, total sleep time, and sleep efficiency. In a multivariate discriminant analysis -- previously shown to distinguish the sleep records of depressed patients from those of normal controls and insomniac patients -- the records from baseline nights were selected as normal and those after scopolamine as predominately depressed. Those observations suggest that muscarinic supersensitivity in normals may function as a pharmacological model for the sleep disturbances of depression. 20 references. (Author abstract modified)

001986 Rimón, Ranán; Kampman, Reima; Viukari, Matti. 10 Hagdud Haivri, Raanana, Israel **Propranolol in the treatment of neurocirculatory asthenia -- an open pilot study.** *Israel Annals of Psychiatry and Related Disciplines.* 17(2):144-148, 1979.

In an open pilot study, 36 patients with neurocirculatory asthenia were treated with propranolol, 80 to 120mg/day for 2 to 4 weeks. Both somatic and mental symptoms were markedly reduced. Significant improvements were found in depressed mood, sleep onset difficulty, interest, palpitations, vertigo, dyspnea, blushing, sweating, tension headache, sighing, dryness of mouth, insomnia, vomiting, and weight loss. The beta-receptor sensitivity found in neurocirculatory asthenia is discussed in relation to the mechanism of action of propranolol. 22 references. (Author abstract modified)

001987 Sarteschi, P.; Cassano, G. B.; Levine, J. Istituto Clinica Psichiatrica, Università di Pisa, Via Roma 67, I-56100 Pisa, Italy **Clinical trials in psychopharmacology: scientific and ethical issues.** *Progress in Neuro-Psychopharmacology.* 3(1-3):293-296, 1979.

Scientific and ethical issues involving clinical trials in psychopharmacology are reviewed. It is noted that the ethical and scientific use of medicines rests upon proof that the medicines to be used are effective and safe for the condition to be treated. The use of the clinical trial is the method by which such evidence is produced. Recent activities by some to decry clinical trials as unethical and to restrict their conduct results in the unacceptable situation of withholding potentially valuable treatments from patients or subjecting patients to the unnecessary risks of treatments not proven safe and efficacious. These actions can lead to a new dark age of chemotherapeutic bloodletting and purgatives under the guise of higher ethical purpose. (Author abstract modified)

001988 Sheehan, David V.; Ballenger, James; Jacobsen, Gary. Psychosomatic Medicine Clinic, Massachusetts General Hospital, Fruit Street, Boston, MA 02114 **Treatment of endogenous anxiety with phobic, hysterical, and hypochondriacal symptoms.** *Archives of General Psychiatry.* 37(1):51-59, 1980.

In a double-blind, placebo controlled, 3 month study, 57 patients severely disabled by endogenous anxiety (anxiety hysteria, agoraphobia with panic attacks) with phobic, hysterical, and hypochondriacal symptoms for a mean period of 13 years were administered imipramine hydrochloride, phenelzine sulfate, or placebo. Patients were also seen in supportive therapy every 2 weeks. Patients in the phenelzine and imipramine cells showed significant improvement over patients in the placebo group and over baseline on all outcome measures. The persistent trend for phenelzine to be superior to imipramine achieved significance only on the Work and Desirability Scale and the Symptom Severity and Phobic Avoidance Scale. Implications for classification and theory are discussed. 30 references. (Author abstract modified)

001989 Wickstrom, E.; Giercksky, K. -E. Ulleval Hospital, Dept. III, University of Oslo, Oslo 1, Norway **Comparative study of zopiclone, a novel hypnotic, and three benzodiazepines.** *European Journal of Clinical Pharmacology.* 17(2):93-99, 1980.

The hypnotic effect and tolerance of the new compound zopiclone 7.5mg, nitrazepam 5mg, flurazepam 30mg, flunitrazepam 2mg, and placebo were compared in a 1 night double-blind study of 414 hospitalized patients who were to undergo an operation on the following day. Zopiclone was slightly superior to nitrazepam but was inferior both to flurazepam and flunitrazepam. All the active drugs differed clearly from placebo. Results from a subset of patients, excluding those who felt anxious either before treatment on the evening prior to the operation or on the following morning, were analyzed separately. All the active products differed significantly from placebo; zopiclone was slightly less effective than the three benzodiazepines. All the benzodiazepines decreased the percentage of patients feeling

anxious about the operation by about 25%, zopiclone by about 10% and placebo did not change it at all. 5 references. (Author abstract)

001990 Wong, David T.; Bymaster, Frank P.; Chen, Sue; Molloy, Bryan B. Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN 46206 **N,N-dimethyl-alpha-(2-p-toloxyl)ethyl benzylamine hydrochloride (LY125180): effects on serotonin uptake and serotonin synthesis in rat brain in vitro and in vivo.** *Biochemical Pharmacology.* 29(6):935-941, 1980.

A new bicyclic compound, LY125180, is described, along with its properties as a selective blocker of serotonin uptake in vitro and in vivo. LY125180 competitively inhibited the uptake of serotonin and norepinephrine by cortical synaptosomes and of dopamine by striatal synaptosomes with K_i values of 0.06, 2.2 and 2.5 μ M respectively. LY125180 blocked serotonin uptake in human platelets by 50% at 22 nM, and reduced serotonin uptake by rat hypothalamic synaptosomes with maximum effect within 1 hour. Prior treatment with an inhibitor of microsomal metabolism enhanced the potency of LY125180 threefold and prolonged its action for at least 4 hours. LY125180 in vivo blocked the neurotoxic effect of p-chloroamphetamine on serotonin uptake by cortical synaptosomes but did not prevent the neurotoxic effect of 6-hydroxydopamine on norepinephrine uptake by hypothalamic synaptosomes or the accumulation of radiolabeled norepinephrine in rat heart. A reduction in brain level of 5-hydroxyindoleacetic acid but not of serotonin and tryptophan and a decrease in the conversion of (3H) tryptophan to (3H)serotonin and (3H)-5-hydroxyindoleacetic acid after the administration of LY125180 suggest a decrease of serotonin turnover in rat brain. These data are consistent with the conclusion that LY125180 is effective and selective in the blockade of the serotonin pump in vitro as well as in vivo. Except for a much shorter duration of action in vivo, LY125180 exhibits properties similar to the earlier reported selective serotonin uptake inhibitor, fluoxetine. 29 references. (Author abstract modified)

001991 Zitrin, Charlotte Marker; Klein, Donald F.; Woerner, Margaret G. Dept. of Psychiatry, Long Island Jewish-Hillside Medical Center, Box 38, Glen Oaks, NY 11004 **Treatment of agoraphobia with group exposure in vivo and imipramine.** *Archives of General Psychiatry.* 37(1):63-72, 1980.

In a randomized double-blind study, 76 White agoraphobic women, 21 to 45 years old, were treated with a combined group exposure in vivo and imipramine or placebo. A majority of the patients in both the placebo and imipramine groups showed moderate to marked improvement. However, imipramine was significantly superior to placebo on three of four reported measures of improvement: primary phobia, spontaneous panic, and global improvement. There was a negative correlation between depression and outcome, with the more depressed patients faring worse on several outcome measures than those who were less depressed. A comparison of these women with agoraphobic women previously treated with imipramine and imaginal desensitization showed a superiority of exposure in vivo midway in treatment, but no significant difference at the completion of therapy. 38 references. (Author abstract)

08 DRUG TRIALS IN SCHIZOPHRENIA

001992 Angrist, B.; Rotrosen, J.; Gershon, S. Neuropsychopharmacology Research Unit, Dept. of Psychiatry, New York University Medical Center, 550 First Ave. New York, NY 10016 **Responses to apomorphine, amphetamine, and neuroleptics in schizophrenic subjects.** *Psychopharmacology.* 67(1):31-38, 1980.

Twenty-one schizophrenic Ss, who had been neuroleptic free, were tested for responsiveness to dopaminergic agonists; apomorphine emesis threshold was determined and change in psychopathology after .05mg/kg d-amphetamine orally was rated. Ss' subsequent responses to neuroleptic treatment were also determined. Sensitivity to apomorphine emesis was also determined in a nonschizophrenic control group. Apomorphine emesis threshold was not significantly different in the schizophrenic and control groups. Correlations between baseline psychopathology, apomorphine sensitivity, and changes in psychopathology after amphetamine and after neuroleptic treatment are reported. On the Brief Psychiatric Rating Scale, baseline psychopathology correlated with improvement after neuroleptics and, on the clinical global impressions, increase of psychopathology after amphetamine also correlated with improvement after neuroleptic treatment. An inverse correlation was found between several indices of sensitivity to amphetamine (psychopathology change) and emetic sensitivity to apomorphine. Examination of individual Ss' responses to amphetamine and, subsequently, neuroleptics, suggests that in the absence of significant clinical change after amphetamine, a brisk therapeutic response to neuroleptics is rare. 29 references. (Author abstract)

001993 Bastrup, P. C.; Christiansen, C.; Transbol, I. Glostrup Hospital, DK-2600 Glostrup, Denmark **Calcium metabolism in schizophrenic patients on long-term neuroleptic therapy.** *Neuropsychobiology*. 6(1):56-59, 1980.

The bone mineral content (BMC) in both forearms (highly related to total body calcium) was measured in a large group of schizophrenic patients receiving neuroleptic drugs. The mean BMC value was 86% of normal, and the decrease was independent of the type of neuroleptic treatment. In contrast, the biochemical variables (serum calcium, magnesium, phosphate, and alkaline phosphatases) were virtually normal. This combination of osteopenia and normal biochemical variables suggests that schizophrenics have osteoporosis, either due to the disease or to the treatment given. 7 references. (Author abstract modified)

001994 Bacopoulos, N. C.; Spokes, E. G.; Bird, E. D.; Roth, R. H. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Antipsychotic drug action in schizophrenic patients: effect on cortical dopamine metabolism after long-term treatment.** *Science*. 205(4413):1405-1407, 1979.

The concentration of the dopamine metabolites homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid (DOPAC) was measured in cortical and subcortical brain regions obtained at autopsy from schizophrenic and normal subjects matched by sex, age, and autopsy interval. In the brains of deceased schizophrenics who underwent long-term treatment with antipsychotic drugs, the concentration of HVA, a dopamine metabolite, was insignificantly increased in the orbital frontal, cingulate, and temporal tip areas of the cortex, but not in the putamen or the nucleus accumbens. It is reported that concentration of HVA was normal in the brains of schizophrenics who were not treated with antipsychotic drugs. 17 references. (Author abstract modified)

001995 Berger, Philip A.; Watson, Stanley J.; Akil, Huda; Barbas, Jack D. Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA **Prospects for the evaluation of endorphins as psychotropic agents.** *Psychopharmacology Bulletin*. 15(3):33-35, 1979.

The role of endorphins in the etiology and treatment of mental disease is discussed. Therapeutic responses to beta-endorphin have been reported for patients with schizophrenia, schizoaffective disorders, agoraphobia, anxiety neurosis, obsessive-

compulsive neurosis, and depression. Improvements in schizophrenics have also been reported with naloxone (which blocks endogenous opiates) with repeated hemodialysis (when leucine-endorphin was found in the dialysate). Controlled double-blind studies are needed to confirm these suggestive findings.

001996 Bjorndal, N.; Bjerre, M.; Gerlach, J.; Kristjansen, P.; Magelund, G.; Oestrich, I. H.; Waehrens, J. Sect. Hans Mental Hospital, Dept. H, DK-4000 Roskilde, Denmark **High dosage haloperidol therapy in chronic schizophrenic patients: a double-blind study of clinical response, side effects, serum haloperidol, and serum prolactin.** *Psychopharmacology*. 67(1):17-23, 1980.

In a 12 week double-blind study, high dosage versus standard dosage haloperidol therapy was evaluated in 23 male chronic schizophrenic inpatients. The patients were relatively treatment resistant and, in spite of traditional neuroleptic medication, were characterized by moderate to severe degrees of illness. No significant difference in therapeutic effect was found between the two groups as measured by the Brief Psychiatric Rating Scale and global assessment. About half of the patients in both groups improved during the trial. The high dosage group had a greater incidence of side-effects and showed a temporary rise in serum alkaline phosphatase and serum aspartate aminotransferase. There was a positive correlation between dose of haloperidol and serum haloperidol, and between haloperidol dose of up to 80mg/day and serum prolactin. At higher doses prolactin response leveled off. Neither serum haloperidol nor serum prolactin showed any correlation to clinical response. It is concluded that high dosage haloperidol therapy is of very limited value. 37 references. (Author abstract modified)

001997 Bond, C. A.; Salinger, Robert J. Salinger, VA Hospital, 2500 Overlook Terrace, Madison, WI 53705 **Fluphenazine outpatient clinics: a pharmacist's role.** *Journal of Clinical Psychiatry*. 40(12):501-503, 1979.

Experiences with 25 schizophrenic outpatients treated in a pharmacist administered fluphenazine decanoate clinic for periods of up to 1 year are reported. These patients showed a significantly lower rehospitalization rate, a decrease in medication related side-effects, and improvement in functional capacity. Results suggest that the pharmacist, supervised by a psychiatrist, as a primary caregiver can be clinically beneficial to schizophrenic outpatients and may help reduce the cost of treatment. 15 references. (Author abstract modified)

001998 Calil, Helena M.; Avery, David H.; Hollister, Leo E.; Creese, Ian; Snyder, Solomon H. Clinical Psychobiology Branch, NIMH, Building 10, Room 4S239, 9000 Rockville Pike, Bethesda, MD 20205 **Serum levels of neuroleptics measured by dopamine radioreceptor assay and some clinical observations.** *Psychiatry Research*. 1(1):39-44, 1979.

A new dopamine radioreceptor assay was used to measure serum concentrations of neuroleptics during treatment of 58 hospitalized patients of which 47 were diagnosed schizophrenic and 11 manic-depressive. Results of this assay are expressed as chlorpromazine equivalents. Serum concentrations varied with different drugs, with extremely high levels in patients receiving thioridazine or mesoridazine. No detectable serum levels were found in 11 patients, probably either due to low drug doses or non-compliance in taking medication. Best results with the assay were obtained in the 22 patients treated with haloperidol. Serum concentrations of haloperidol were correlated with dose and were related to the Brief Psychiatric Rating Scale (BPRS) total pathology score, as well as to BPRS factor scores for thinking disturbance and paranoid disturbance. Serum concentrations of haloperidol were not different among patients with or without the presence of extrapyramidal symptoms or among patients re-

ceiving or not receiving concurrent antiparkinson medication. 20 references. (Author abstract modified)

001999 Casper, Regina; Garver, David L.; Dekirmenjian, Haroutune; Chang, Sidney; Davis, John M. Illinois State Psychiatric Institute, 1601 W. Taylor St., Chicago, IL 60612 **Phenothiazine levels in plasma and red blood cells: their relationship to clinical improvement in schizophrenia.** *Archives of General Psychiatry.* 37(3):301-305, 1980.

The relationship between steady-state plasma and red blood cell (RBC) concentrations of the phenothiazine derivative, butaperazine maleate, and the therapeutic response in 24 hospitalized schizophrenics who received constant maintenance doses of butaperazine during the first 2 weeks of treatment was investigated. Butaperazine concentrations in RBCs correlated significantly with clinical improvement in an inverted U-shaped pattern, whereas plasma levels were not significantly related to clinical response. Both plasma levels and RBC levels showed large interpatient variations. The level of RBC bound drug may be a better peripheral correlate of drug levels in the brain than are drug levels in plasma. Thus, monitoring drug levels in RBCs may have an advantage over measuring levels in plasma. These findings may not generalize to other antipsychotic agents. 16 references. (Author abstract modified)

002000 Comar, D.; Zarifian, E.; Verhas, M.; Soussaline, F.; Maziere, M. Commissariat à l'Energie Atomique, Département de Biologie, Hôpital d'Orsay, F-91406 Orsay, France **Brain distribution and kinetics of 11C-chlorpromazine in schizophrenics: positron emission tomography studies.** *Psychiatry Research.* 1(1):23-29, 1979.

The in vivo distribution and kinetics of chlorpromazine (CPZ) in the brain of schizophrenic patients was estimated. The positron emitter 11C (20 minutes half-life) permits labeling CPZ and studying its distribution in humans by external counting. Trace amounts of 11C-CPZ were injected intravenously into 22 schizophrenic patients, all untreated for several months with neuroleptics. The brain uptake was 6.04 plus or minus 1.6% of the injected dose 15 minutes after the injection, and it remained constant for 45 minutes. By positron emission tomography, the drug distribution was shown to be in the gray matter; and such structures as the cortex, caudate nucleus, thalamus, and putamen could be identified. This new methodology will be helpful in studying specific receptors in humans in a noninvasive way. 9 references. (Author abstract modified)

002001 Crow, T. J. Division of Psychiatry, Clinical Research Centre, Northwick Park Hospital, Harrow, England HA1 3UJ **Catecholamine reward pathways and schizophrenia: the mechanism of the antipsychotic effect and the site of the primary disturbance.** *Federation Proceedings.* 38(1):2462-2467, 1979.

Evidence suggesting that catecholamine systems related to reward mechanisms (the locus coeruleus system and the dopamine neurons arising from the ventral midbrain) are disturbed in schizophrenia is reviewed. Neuroleptic drugs appear to exert their antipsychotic effects in acute schizophrenia by blocking dopamine receptors, but the time course of the effects suggests the mechanism is more complex than simple reversal of a neurohumoral imbalance. Postmortem studies have shown an increase in postsynaptic receptor density with no change in dopamine turnover, even in patients who had not received medication in the year before death. Present evidence is consistent with the hypothesis that certain psychotic episodes can be controlled by counteracting positive feedback processes subserving positive reinforcement mechanisms. 52 references. (Author abstract modified)

002002 Crow, T. J. Clinical Research Centre, Northwick Park Hospital, Harrow, Middlesex HA1 3UJ, England **What is wrong with dopaminergic transmission in schizophrenia?** *Trends in Neurosciences.* 2(2):52-55, 1979.

The causal relationship between dopamine and schizophrenia is examined and the effects of neuroleptic drugs on this relationship is discussed. The findings of the clinical studies on the mechanism of the antipsychotic effect support the hypothesis that dopamine receptor blocking potency is the only requirement for therapeutic activity. The postmortem studies did not provide evidence that the activity of dopamine neurons is increased in schizophrenia. However, dopamine receptor numbers were increased and this appeared not to be secondary to neuroleptic drug administration. 18 references.

002003 Davis, Glenn C.; Buchsbaum, Monte S.; van Kammen, Daniel P.; Bunney, William E., Jr. Buchsbaum: National Institute of Mental Health, Building 10, Room 2N212, 9000 Rockville Pike, Bethesda, MD 20205 **Analgesia to pain stimuli in schizophrenics and its reversal by naltrexone.** *Psychiatry Research.* 1(1):61-69, 1979.

Psychophysical pain ratings and somatosensory evoked potentials (EPs) were studied in 17 patients with schizophrenia who were off medication and sex matched normal controls. Five of the 17 schizophrenic patients also participated in a clinical trial of naltrexone. In comparison with normal controls, schizophrenic patients were significantly more insensitive to painful stimulation (based on nonparametric analogues of d' from signal detection analysis) and had significantly smaller somatosensory EPs to painful stimuli. Schizophrenics treated with naltrexone showed significant increases in EP amplitude at higher stimulus intensities and hyperalgesic effects on pain ratings. 39 references. (Author abstract)

002004 Davis, Kenneth L.; Hollister, Leo E.; Berger, Philip A. Psychiatry Service, Veterans Administration Medical Center, 130 West Kingsbridge Rd., Bronx, NY 10468 **Choline chloride in schizophrenia.** *American Journal of Psychiatry.* 136(12):1581-1584, 1979.

The possibility that choline chloride might reduce schizophrenic symptoms by increasing central cholinergic activity was investigated. In a single-blind crossover study, up to 20g/day of choline chloride had no significant effect on clinical ratings of nine schizophrenic patients. However, there was some evidence that choline significantly increased symptoms of depression. 36 references. (Author abstract)

002005 Deniker, P.; Loo, H.; Cottureau, M. J. Service universitaire de Santé Mentale, 100, rue de la Santé, F-75014 Paris, France **Parenteral loxapine in severely disturbed schizophrenic patients.** *Journal of Clinical Psychiatry.* 41(1):23-26, 1980.

An uncontrolled open trial of loxapine, a tricyclic antipsychotic drug of the dibenzoxapine class, was performed by intramuscular administration of 50 to 200mg to 28 schizophrenic patients previously refractory to other neuroleptic drugs is reported. Clinical evaluation, the Brief Psychiatric Rating Scale (BPRS), the Nurses' Observation Scale for Inpatient Evaluation, and biological evaluation were performed before and at the eighth day of the treatment. Global clinical evaluation and statistical analysis of BPRS showed the high efficacy of loxapine with a sedative effect during the initial phase and a disinhibiting and hallucinolytic character at a later stage. Tolerance to the preparation appeared good both locally and systematically with the possible exception of transient effects upon body temperature. It is concluded that parenteral loxapine is a highly effective neuroleptic. 16 references. (Author abstract modified)

002006 Deniker, P.; Zarifian, E. Zarifian: Service Hospitalo-Universitaire de Sante Mentale et de Therapeutique, 100-102, rue de la Sante, F-75674 Paris 14, France **Perspectives in chemotherapy of schizophrenic psychoses.** *Progress in Neuro-Psychopharmacology.* 3(1-3):39-45, 1979.

Chemotherapy in the schizophrenic psychoses is reviewed, and the differential effectiveness of chemotherapy in acute and chronic schizophrenia and on different symptoms of schizophrenia is described. A hypothetical ideal antipsychotic drug would have to have different, and sometimes contradictory effects, especially in treating hebephrenic and paranoid symptoms. It is contended that basic perspectives in the chemotherapy of schizophrenic psychoses must be founded on better methodological considerations in clinical trials, on a better use of antipsychotic drugs with the help of pharmacokinetic data and computerized EEG and also on new neurochemical findings. The promise of GABA like, and beta-blocking drugs is noted. 24 references. (Author abstract modified)

002007 Ford, Thomas Walter. University of Texas at Austin **The effects of psychotropic drugs on psychological tests.** (Ph.D. dissertation). Dissertation Abstracts International. 39(7):3511-B, 1979. Ann Arbor, Univ. Microfilms No. 7900559, 89p., 1978.

A study which attempted to remedy deficiencies of previous research on the effect of antischizophrenia psychotropic drugs on psychological tests is reported. Male and female adolescents were assigned to either a drug group or control group and administered a test battery within 36 hours of admission to the hospital. After testing, subjects in the drug group were started on an antischizophrenia drug regimen while control subjects received no drugs. The test battery was readministered 2 days and 10 days after treatment was begun. None of the experimental subjects had decreases after the drug regimen was begun but positive antipsychotic effects leading to an improvement in test scores were not found either. Increases in scores on tests not susceptible to practice effects suggested that testing after a drug regimen is begun may provide more representative test scores. (Journal abstract modified)

002008 Gruzeli, J. H.; Hirsch, S. R.; Weller, M.; Murphy, C. Dept. of Psychiatry, Charing Cross Hospital, Fulham Palace Road, London W.6, England **Influence of D- or DL-propranolol and chlorpromazine on habituation of phasic electrodermal responses in schizophrenia.** *Acta Psychiatrica Scandinavica.* 60(3):241-248, 1979.

The question of whether propranolol in the dextro form shares the properties of the racemate in facilitating habituation of the electrodermal response was investigated. It was found that dextro propranolol shared the properties of the racemate in facilitating habituation of the electrodermal orienting reflex in schizophrenic patients. This effect appeared independent of influences on levels of skin conductance and nonspecific responses. Chlorpromazine did not normalize orienting activity. If the findings from open clinical studies that D-propranolol has anti-psychotic properties are confirmed, the fact that dextro propranolol has only minimal cardiovascular effects may give it important advantages as an anti-psychotic agent. Controlled clinical studies to prove its therapeutic action and neurobiological studies to determine its central mechanisms of action are warranted. 20 references. (Author abstract modified)

002009 Hogarty, Gerard E.; Schooler, Nina R.; Ulrich, Richard; Mussare, Frank; Ferro, Peregrino; Herron, Eileen. 3811 O'Hara Street, Pittsburgh, PA 15261 **Fluphenazine and social therapy in the aftercare of schizophrenic patients: relapse analyses of a two-year controlled study of fluphenazine decanoate and flu-**

phenazine hydrochloride. *Archives of General Psychiatry.* 36(12):1283-1294, 1979.

In a study of the ability of long acting fluphenazine decanoate and oral fluphenazine hydrochloride to forestall relapse among newly discharged schizophrenics receiving low or high degrees of social therapy (ST), 105 patients were randomly assigned to various treatments and maintained under controlled conditions for 2 years or until relapse. Relapse rates for all treatments remained traditionally high. Relapse rates for both drug forms were nearly identical for the first year, indicating that drug non-compliance does not adequately explain schizophrenic relapse. However, schizophrenics who received fluphenazine decanoate and ST had a reduced risk of relapse over time. Relapsers who received fluphenazine decanoate appeared more affectively disturbed than other relapsers, yet both groups were diagnostically and symptomatically equivalent prior to treatment. Personal discomfort and intrafamilial stress were important predictors. 49 references. (Author abstract modified)

002010 Magelund, G.; Gerlach, J.; Casey, D. E. Psychiatric Department E, Sct. Hans Mental Hospital, DK-4000 Roskilde, Denmark **Neuroleptic-potentiating effect of alpha-methyl-p-tyrosine compared with haloperidol and placebo in a double-blind cross-over trial.** *Acta Psychiatrica Scandinavica.* 60(2):185-189, 1979.

The neuroleptic potentiating role of alpha-methyl-p-tyrosine (AMPT), a tyrosine hydroxylase inhibitor, was compared with haloperidol and placebo in a double-blind crossover trial with schizophrenic patients. Both AMPT and haloperidol increased the anti-schizophrenic effect of neuroleptic treatment in reduced dose compared with placebo (P less than 0.05), though two patients relapsed during the AMPT period. Both drugs slightly increased extrapyramidal symptoms, but the effect was greater with haloperidol. The limited antipsychotic effect and the potential for aggravating neurological symptoms suggest that the combination of AMPT and neuroleptics does not offer a superior advantage to treating schizophrenia. AMPT, however, may still be used as a research tool in elucidating pathogenetic mechanisms. 14 references. (Author abstract modified)

002011 Meadow, Arnold; Donlon, Patrick; Wahba, Michel; Tupin, Joe P. Section of Clinical Psychology, Dept. of Psychiatry, University of California, Davis, Medical Center, Sacramento, CA 95817 **An experimental test of two opposing theories of the perception deficit in schizophrenia.** *Journal of Clinical Psychology.* 35(4):707-712, 1979.

Two alternate theories of the etiology of the perceptual defect in schizophrenia were tested: Searles' and Hartmann's theory that it is a secondary reaction to defense and McGhie's theory that it is a primary defect. Results indicated that patients administered high as compared to patients administered low dosages of fluphenazine HCL performed significantly better on two digit span tests, the test comprised of words with emotional content presented with neutral affect, and the test with no distracting stimuli. Because the higher dosage did not produce greater improvement on the test that utilized emotional distracting stimuli than on the test accompanied by no distracting stimuli, the results are interpreted as supporting the theory of McGhie. 5 references. (Author abstract modified)

002012 Pfefferbaum, Adolf; Berger, Philip A.; Elliott, Glen R.; Tinklenberg, Jared R.; Kopell, Bert S.; Barchas, Jack D.; Li, Choh Hao. Psychiatry Service, 116A3, VA Medical Center, Palo Alto, CA **Human EEG response to beta-endorphin.** *Psychiatry Research.* 1(1):83-88, 1979.

Beta-endorphin, morphine, and saline were given intravenously to a single schizophrenic subject on separate occasions in a

double-blind design. EEG spectral analyses performed on data collected before and after drug injection demonstrated that beta-endorphin and morphine produced similar increases in alpha power within 5 to 15 minutes after injection. This effect could be distinguished from two placebo (saline injections). These data suggest that intravenous beta-endorphin can produce changes in the central nervous system in humans. 17 references. (Author abstract)

002013 Pinto, R.; Bannerjee, A.; Ghosh, N. Dept. of Psychiatry, Luton and Dunstable Hospital, Luton, Bedfordshire LU4 0D2, England LU4 0D2 **A double-blind comparison of flupenthixol decanoate and fluphenazine decanoate in the treatment of chronic schizophrenia.** *Acta Psychiatrica Scandinavica*. 60(4):313-322, 1979.

Sixty-four chronic stabilized schizophrenics were studied for 18 months in order to assess the possible difference in therapeutic effects and side-effects between flupenthixol decanoate and fluphenazine decanoate. Although certain differences in the BPRS sub scores in favor of flupenthixol were present at various stages in the study, there was no significant difference between the two drugs in the overall antipsychotic scores at the end of the assessment period. However, more patients on fluphenazine required additional therapy for depression or anxiety during the trial period. 12 references. (Author abstract)

002014 Rinieris, P.; Christodoulou, G. N.; Souvatzoglou, A.; Koutras, D. A.; Stefanis, C. Dept. of Psychiatry, Athens University Medical School, Eginition Hospital, 74 Vas. Sophias Avenue, Athens 611, Greece **Free-thyroxine index in schizophrenic patients before and after neuroleptic treatment.** *Neuropsychobiology*. 6(1):29-33, 1980.

The mean values of serum thyroxine (T4) in vitro radioactive triiodothyronine uptake and free thyroxine index (FTI) in 41 drug free schizophrenic patients were determined. The values did not differ significantly from those of euthyroid controls. Following 6 weeks of treatment of 24 schizophrenics with chlorpromazine, trifluoperazine, or clozapine, a significant decrease in serum T4 and FTI was noted after chlorpromazine and clozapine, whereas after trifluoperazine only serum T4 decreased, but not FTI. The questions arising from these findings are discussed and the need for a future investigation of serum triiodothyronine and serum thyroid stimulating hormone in schizophrenic patients before and after neuroleptic treatment is stressed. 21 references. (Author abstract modified)

002015 Rosenblatt, J.; Parry, R.; Bigelow, L.; DeLisi, L.; Wagner, R.; Kleinman, J.; Weinberger, D.; Potkin, S.; Shilling, D. William A White Bldg., Room 528, Saint Elizabeths Hospital, Washington, DC 20032 **Measurement of serum neuroleptic concentrations by radioreceptor assay: concurrent assessment of clinical response and toxicity.** (Unpublished paper). Washington, DC, NIMH, 1980. 51 p.

To determine whether plasma or serum dopamine receptor blocking activity correlates closely with the clinical therapeutic and toxic effects of neuroleptic drugs, the relationship between serum neuroleptic concentrations, as measured by radioreceptor assay, and clinical response was studied in schizophrenic patients. It was found that the neuroleptic radioreceptor assay is sensitive, reliable, and appropriate for the study of neuroleptic serum concentration and clinical response. Neuroleptic serum concentration is positively correlated with dose, and plasma prolactin is positively correlated with neuroleptic serum level. Neuroleptic serum concentration is higher in elderly patients despite treatment with relatively lower doses and is lower in patients treated conjointly with anti-Parkinsonian medication. Onset of extrapyramidal side-effects is associated with relatively

low serum neuroleptic concentrations. Tardive dyskinesia patients had higher serum neuroleptic concentrations than an age matched and dose matched group of control patients. Serum neuroleptic concentration was negatively correlated with both anxiety/depression and thought disorder cluster ratings of the BPRS, but only in patients treated with neuroleptic for at least 14 days. 62 references.

002016 Rosenblatt, Jack E.; Lake, C. Raymond; Van Kammen, Daniel P.; Ziegler, Michel G.; Bunney, William E., Jr. Lake: National Institute of Mental Health, Building 10, Room 2S243, 9000 Rockville Pike, Bethesda, MD 20205 **Interactions of amphetamine, pimozone, and lithium on plasma norepinephrine and dopamine-beta-hydroxylase in schizophrenic patients.** *Psychiatry Research*. 1(1):45-52, 1979.

The effects of intravenous amphetamine on plasma levels of norepinephrine (NE) dopamine-beta-hydroxylase (DBH), pulse rate, and blood pressure was studied in schizophrenic patients. Amphetamine increased plasma NE, pulse rate, and blood pressure without significantly changing plasma DBH. DBH activity was similar in drug free schizophrenic and normal subjects. Neither pimozone nor lithium altered these amphetamine effects nor changed any of the cardiovascular parameters measured in the drug free subjects. Pimozone and lithium alter behavior and the behavioral effects of amphetamine, but neurotransmitters other than NE may be involved. 33 references. (Author abstract modified)

002017 Schooler, Nina R.; Levine, Jerome; Severe, Joanne B.; Brauzer, Benjamin; DiMascio, Alberto; Klerman, Gerald L.; Tuason, Vicente B. Psychopharmacology Research Branch, NIMH, 5600 Fishers Lane, Rockville, MD 20857 **Prevention of relapse in schizophrenia: an evaluation of fluphenazine decanoate.** *Archives of General Psychiatry*. 37(1):16-24, 1980.

The role of guaranteed delivery of medication in the prevention of relapse and the enhancement of community adjustment was examined in 290 newly hospitalized schizophrenic patients in four hospitals. Patients were randomly assigned to groups receiving either long-acting injectable fluphenazine decanoate or short acting oral fluphenazine hydrochloride. After discharge and stabilization, patients were treated in the community for up to 1 year. By the end of the year, 28% of all patients had relapsed. Contrary to hypothesis, differences between the two groups in relapse percentages were not significant. Further, there were no differences between treatment groups as to development of affective symptomatology or social adjustment. Patients who rated themselves as having more symptom distress at the start of the community maintenance phase of study relapsed much earlier while receiving fluphenazine decanoate rather than fluphenazine hydrochloride. Results suggest that compliance is not an important determinant among newly discharged schizophrenic patients. 21 references. (AUTHOR ABSTRACT MODIFIED)

002018 Simpson, George M.; Cooper, Thomas B.; Bark, Nigel; Sud, Indu; Lee, J. Hillary. Cooper: Rockland Research Institute, Orangeburg, NY 10962 **Effect of antiparkinsonian medication on plasma levels of chlorpromazine.** *Archives of General Psychiatry*. 37(2):205-208, 1980.

The effects of trihexyphenidyl hydrochloride on plasma chlorpromazine levels in a group of chronic schizophrenic patients were examined. Twenty-one chronic schizophrenics were stabilized with chlorpromazine therapy at their therapeutic dosage for one month. Trihexyphenidyl hydrochloride or identical placebo was then added according to a double-blind, split crossover design. Steady-state blood samples were drawn three times weekly during the experimental period and the amount of

chlorpromazine was determined. The results indicated there were no differences in the levels obtained between the trihexyphenidyl and the placebo phases. A two hour postdrug blood sample was also drawn at the end of each phase and again, there were no differences between the two conditions. 16 references. (Author abstract modified)

002019 Simpson, Lance L. Dept. of Pharmacology, College of Physicians and Surgeons, Columbia University, 630 West 168th St., New York, NY 10032 Combined use of molindone and guanethidine in patients with schizophrenia and hypertension. *American Journal of Psychiatry*. 136(11):1410-1414, 1979.

The combined use of molindone and guanethidine in patients with concomitant schizophrenia and hypertension was examined with in vitro studies of seven patients. There was no evidence of an adverse drug interaction. The data indicate that molindone and guanethidine can be used in combination safely and effectively. It is concluded that this work should ultimately lead to the elimination of hypertensive crises as a possible consequence of the administration of monoamine oxidase inhibitors. 13 references. (Author abstract modified)

002020 Siris, Samuel G.; Siris, Ethel S.; van Kammen, Daniel P.; Docherty, John P.; Alexander, Paul E.; Bunney, William E., Jr. Dept. of Psychiatry, Mount Sinai Hospital, One Gustave Levy Pl., New York, NY 10024 Effects of dopamine blockade on gonadotropins and testosterone in men. *American Journal of Psychiatry*. 137(2):211-215, 1980.

The effects of neuroleptic medication on the hypothalamic-pituitary gonadal axis in schizophrenic males were investigated. Plasma luteinizing hormone (LH), prolactin, and testosterone were initially normal in nine acutely psychotic males with schizophrenia or schizoaffective disorder, while follicle stimulating hormone (FSH) was normal in eight of the nine Ss. Following treatment with pimozide, a dopamine receptor blocker, significant declines occurred in FSH and LH although levels remained within normal limits. Prolactin rose significantly, but testosterone did not change. These reductions are consistent with the hypotheses that dopamine and/or prolactin are involved in gonadotropin secretion. The maintenance of normal levels of gonadotropins and testosterone, however, suggests that these Ss possess relatively normal hypothalamic-pituitary gonadal axis function before and during neuroleptic treatment. 26 references. (Author abstract modified)

002021 Tuma, A. Hussain; May, Philip R. A. Clinical Research Branch, NIMH, ADAMHA, 5600 Fishers Lane, Room 10C-24, Rockville, MD 20857 And if that doesn't work, what next...? A study of treatment failures in schizophrenia. *Journal of Nervous and Mental Disease*. 167(9):566-571, 1979.

An evaluation of the effectiveness of group psychotherapy combined with ataraxic drugs in the treatment of schizophrenia is presented. A systematic study of schizophrenic patients who did not respond satisfactorily to one of five different forms of treatment given under controlled conditions showed that almost all of them responded satisfactorily to subsequent treatment with the combination of ataraxic drugs and group psychotherapy. Whatever the original form of treatment, and despite subsequent retreatment with drugs and group psychotherapy, there was a treatment resistant core -- a few patients who either responded very slowly or who improved relatively little. 5 references. (Author abstract modified)

002022 Tune, Larry E.; Creese, Ian; Coyle, Joseph T.; Pearlson, Godfrey; Snyder, Solomon H. Snyder: Johns Hopkins University School of Medicine, Baltimore, MD 21205 Low neuroleptic serum levels in patients receiving fluphenazine decanoate. *American Journal of Psychiatry*. 137(1):80-82, 1980.

Serum levels of fluphenazine in nine schizophrenic patients were monitored following injections of fluphenazine decanoate ranging from 10 to 75mg. Levels were detected by a radioreceptor assay based on the ability of the rat caudate membranes. Serum levels of fluphenazine were quite stable over a 2 to 3 week period following single intramuscular injections of the decanoate and correlated with injected dose. Following decanoate treatment serum levels of fluphenazine were substantially lower than levels observed for most other neuroleptics administered orally. Questions as to how fluphenazine decanoate can exert therapeutic actions are considered. 18 references. (Author abstract)

002023 van Kammen, Daniel P. Sect. on Neuropsychopharmacology, Biological Psychiatry BrBr., NIMH, Building 10, Room 4N214, 9000 Rockville Pike, Bethesda, MD 20205 The dopamine hypothesis of schizophrenia revisited. *Psychoneuroendocrinology*. 4(1):37-46, 1979.

Although clinical studies seem to support the dopamine (DA) hypothesis of schizophrenia, evidence from biochemical studies had been inconclusive. Schizophrenic symptoms fluctuate with central DA activity, and some brain autopsies support the notion of dysfunctional DA systems in schizophrenics. However, increasing evidence indicates that other neurotransmitters or modulators of DA activity, such as amino acids (GABA), amines (norepinephrine), and peptides (endorphins), may be involved in the regulation of psychosis. The development of more specific presynaptic DA agonists and other agents that specifically affect mesolimbic DA systems could further elucidate the role of DA in schizophrenia. 63 references. (Author abstract modified)

002024 van Kammen, Daniel P.; Docherty, John P.; Marder, Stephen R. Biological Psychiatry Branch, NIMH, Bldg 10, Rm 4N214, 9000 Rockville Pike, Bethesda, MD 20205 Lack of behavioral supersensitivity to d-amphetamine after pimozide withdrawal. *Archives of General Psychiatry*. 37(3):287-290, 1980.

The postulated relationship between psychotic decompensation as observed after d-amphetamine infusion and the dopamine receptor supersensitivity expected to be present during the neuroleptic withdrawal period were examined in 12 schizophrenic patients. A 20mg i.v. dose of d-amphetamine did not cause a stronger psychotogenic effect. One week after discontinuation of pimozide treatment, the d-amphetamine-induced change was not significantly different from the response to a similar infusion during the drug free state. Unexpectedly, the increase in Brief Psychiatric Rating Scale mannerisms (paranoid disturbance cluster score) and posturing item and in the pulse rate response to d-amphetamine were decreased. The results question the role of dopamine in d-amphetamine effects and suggest postneuroleptic dopamine receptor sensitivity. Results challenge a simple dopamine hypothesis of schizophrenia. 41 references. (Author abstract modified)

002025 Weinberger, Daniel R.; Bigelow, Llewellyn B.; Kleinman, Joel E.; Klein, Susan T.; Rosenblatt, Jack E.; Wyatt, Richard J. Laboratory of Clinical Psychopharmacology, Div. of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC 20032 Cerebral ventricular enlargement in chronic schizophrenia: an association with poor response to treatment. *Archives of General Psychiatry*. 37(1):11-13, 1980.

Response to neuroleptic drug treatment in ten chronic schizophrenic patients with enlarged cerebral ventricles was compared with that of ten similar patients with normal ventricles. The groups were closely matched for age, age of onset of illness, duration of illness and hospitalization, drug dosage, and plasma neuroleptic concentration as measured by radioreceptor assay.

Response was significantly worse in patients with enlarged ventricles. This finding supports the notion that ventricular enlargement is clinically relevant in patients with chronic schizophrenia, and that patients with this abnormality may have a biologically different illness than similar patients without it. 21 references. (UTHOR ABSTRACT)

002026 Woggon, Brigitte; Fleischhauer, J.; Widmer, A. Psychiatrische Universitätsklinik Zurich, Forschungsdirektion, Lenggstrasse, 31, Postfach 68, CH-8029 Zurich, Switzerland / **The influence of diagnosis, hospital and sex on the effects on bromperidol.** Der Einfluss von Diagnose, Klinik und Geschlecht auf die Wirkung von Bromperidol. International Pharmacopsychiatry. 14(4):213-227, 1979.

Data from the AMP findings from 78 schizophrenics participating in four clinical trials were examined for the effects of bromperidol. A strong antipsychotic effect with an early onset, little sedation, good improvement of accompanying depressive symptoms, little autonomic but strong extrapyramidal side-effects were noted. No differences occurred between the effects in men and women. Differences between patient populations in two hospitals were small in comparison to those between patients with catatonic and paranoid schizophrenia. In the former Ss, bromperidol had a stronger antipsychotic effect and showed an earlier evidence of its effects. 22 references. (Journal abstract modified)

002027 Young, Michael A.; Meltzer, Herbert Y. Illinois State Psychiatric Institute, 1601 W. Taylor Street, Chicago, IL 60612 **The relationship of demographic, clinical, and outcome variables to neuroleptic treatment requirements.** Schizophrenia Bulletin. 6(1):88-101, 1980.

Sixty-one acute schizophrenic patients were examined retrospectively to determine whether any demographic, clinical, and outcome characteristics distinguished patients who improved with placebo or low dosages of antipsychotics (PLD patients) from patients who required high conventional dosages of antipsychotics (HCD patients). Prominent excitement and certain somatic and auditory hallucinations were significantly more frequent in the HCD patients. PLD patients were more likely to be female, were hospitalized more rapidly after the onset of psychosis, and were more often first admissions. Nonschizoid patients who were nonparanoid tended to be in the PLD group while nonschizoid patients who were paranoid tended to be in the HCD group. PLD patients were less psychotic at discharge, remained out of the hospital for longer periods, and had fewer rehospitalizations. These results confirm other reports of better outcome for patients successfully treated without medication. 36 references. (Author abstract modified)

002028 Young, Michael A.; Meltzer, Herbert Y. Meltzer: Dept. of Psychiatry, University of Chicago Pritzker School of Medicine, 950 East 59th Street, Chicago, IL 60637 **RMI-81,582, a novel antipsychotic drug.** Psychopharmacology. 67(1):101-106, 1980.

RMI-81,582 (2-chloro-11-(3-dimethylaminopropylidene morphanthridene), a potential antipsychotic agent, was administered to eight chronic and four acute male schizophrenics in an open label study. Ten of twelve patients improved, particularly those who were experiencing their first hospitalization, regardless of whether they met research diagnostic criteria for acute or chronic schizophrenia. Significant improvement was noted on the Clinical Global Impressions and Brief Psychiatric Rating Scale. No extrapyramidal side-effects were noted and other adverse reactions were few. Serum prolactin levels, a measure of antidopaminergic activity, were increased by low moderate dosages of RMI-81,582 in seven of 11 patients. Four patients had no

increase in serum prolactin with RMI-81,582. In six of the seven patients who developed increases in serum prolactin, prolactin levels returned to those characteristic of the placebo period as the dosage of RMI-81,582 was increased. With classical neuroleptics, serum prolactin levels increase as the dose increases up to approximately the equivalent of chlorpromazine 600mg/day and then remain fairly constant. The pattern of serum prolactin response in both man and laboratory animals and the absence of extrapyramidal side-effects suggest RMI-81,582 may have a clozapine-like action. 27 references. (Author abstract)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

002029 Abe, Kazuhiko. Dept. of Psychiatry, University of Occupational & Environmental Health, Medical School, Yahata-Nishiku 807, Japan **Treatment of paranoid depressives and depressive school phobic children.** International Pharmacopsychiatry. 14(2):110-113, 1979.

Treatment of paranoid depressives and depressed school phobic children in a Japanese university hospital is briefly reported. Data are presented on the effectiveness of sulpiride, a benzamide which has antidepressant and anxiolytic effects in low doses, in treating both classes of patients. 5 references.

002030 Ananth, J.; Engelsmann, F.; Kiriakos, R.; Kolivakis, T. Allan Memorial Institute, 1025 Pine Avenue West, Montreal, PQ, Canada **Prediction of lithium response.** Acta Psychiatrica Scandinavica. 60(3):279-286, 1979.

Clinical and familial genetic predictors of lithium response were investigated. Females, patients with prior manic episodes, initial onset of illness with a manic episode, and premorbid psychopathic personality were all indicators of favorable long-term lithium response. Patients with retarded depression, severe anxiety, thought disorder and those with higher scores on the Psychopathic Deviate and Paranoia scales of the MMPI were poor lithium responders. However, only a few of the differences between responders and nonresponders were statistically significant. Results suggest a number of predictive variables for the identification of lithium responders. 20 references. (Author abstract modified)

002031 Arato, Mihaly; Rihmer, Zoltan; Felszeghy, Klara. National Institute for Nervous and Mental Diseases, Budapest, Hungary **Reduced plasma cyclic AMP level during prophylactic lithium treatment in patients with affective disorders.** Biological Psychiatry. 15(2):319-322, 1980.

The plasma cyclic AMP level during lithium (Li) treatment was examined in 46 euthymic patients with affective disorders. Nine patients received low doses of neuroleptics in addition to Li, three were given antidepressants, and six patients took hypnotics at night. There was a control group of 19 healthy subjects. Plasma cAMP levels exhibited a significant decrease in patients treated with Li relative to the control group. No differences in mean cAMP level were found between sexes or between patients who were given additional drugs. It is suggested that the inverse correlation found between Li and cAMP levels suggests that the decrease in cAMP level could be a result of Li treatment. 19 references.

002032 Asnis, G. M.; Nathan, R. S.; Halbreich, U.; Halpern, F. S.; Sachar, E. J. Dept. of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY 10032 **TRH tests in depression.** Lancet. No. 8165:424-425, 1980.

Results of a study of thyrotropin response to the thyrotropin releasing hormone (TRH) test in 13 patients (10 male, 3 female) with primary unipolar depression and five patients with secondary depression (3 females, 2 males) are reported in a letter to the

editor. All patients tested were severely depressed but medically healthy. Following 10 drug free days, blood samples were taken prior and for 60 minutes after infusion with 500 mugram TSH. Subjects were retested after full clinical recovery while on antidepressants. During illness there were no significant differences between T3, T4, and TSH between groups. However, unipolar patients had significantly smaller TSH responses than did those with secondary depression both during illness and after clinical recovery. Thus, TSH response to TRH differentiated primary unipolar depression from secondary depression and this distinction may continue in depressive subtypes regardless of remission. Data suggest the value of the TRH test as a marker of vulnerability to primary unipolar depressive illness. 4 references.

002033 Ban, Thomas A. Dept. of Psychiatry, Vanderbilt University, Nashville, TN **Amoxapine and viloxazine: review of the literature with special reference to clinical studies.** *Psychopharmacology Bulletin*. 15(3):22-25, 1979.

The literature on amoxepine and viloxazine is reviewed, with emphasis on clinical studies. Papers published in the last 10 years suggest that both drugs have antidepressant effects in the dose range of 150 to 300mg/day. Both drugs reportedly have a more rapid onset of action than other antidepressants currently available, but the evidence for this is inconclusive. Both drugs appear to have less frequent and severe side-effects than reference antidepressants, but nausea and vomiting appear to be more common with viloxazine than with other antidepressant drugs.

002034 Beckmann, Helmut; Athen, Dieter; Olteanu, Margit; Zimmer, Reinhold. Zentralinstitut für Seelische Gesundheit, J 5, D-6800 Mannheim, Germany **DL-phenylalanine versus imipramine: a double-blind controlled study.** *Archiv für Psychiatrie und Nervenkrankheiten*. 227(1):49-58, 1979.

In a double-blind study, DL-phenylalanine (150-200mg/24h) or imipramine (150-200mg/24h) was administered to 40 depressed patients for 30 days. The AMP system, the Hamilton Depression Scale and the Bf-S self-rating questionnaire were used to document psychopathological, neurologic, and somatic changes. Twenty-seven patients completed the 30 day trial. No statistical difference could be found between these two drug treatment groups using the Hamilton Depression Scale and the Bf-S self-rating questionnaire. Ratings for anxiety were significantly lower in the imipramine group on days 10 and 20, but not on day 30; in addition sleep disturbances were more influenced by imipramine on days 1, 5, and 10 but not on days 20 and 30. Separate analysis of psychopathological syndromes as somatic depressive syndrome and retarded depressive syndrome did not show a group difference. It is concluded that DL-phenylalanine might have substantial antidepressant properties. 24 references. (Journal abstract)

002035 Bjorum, N.; Kirkegaard, C. Psychiatric Dept. D, Frederiksberg Hospital, DK-2000 Copenhagen F, Denmark **Thyrotropin-releasing-hormone test in unipolar and bipolar depression.** *Lancet*. No. 8144:694, 1979.

The thyrotropin (TSH) responses to thyrotropin releasing hormone (TRH) of 35 patients with unipolar endogenous depression and 21 patients with bipolar endogenous depression were compared. The patients were all euthyroid without endocrine diseases and had been off lithium therapy for at least 6 months. No significant differences in basal serum TSH levels or responses to TRH between the two groups were found. The data do not suggest that the TSH response to TRH will be of value in the differential diagnosis of unipolar and bipolar depression; nor do they support the notion that different neuroendo-

crine mechanisms are operating in these two conditions. 3 references.

002036 Bloomingdale, Lewis M.; Bressler, Bernard. 28 Fairview Rd., Scarsdale, NY 10583 **Rapid intramuscular administration of tricyclic antidepressants.** *American Journal of Psychiatry*. 136(8):1092-1093, 1979.

A five step routine for the intramuscular administration of tricyclic medication and the ensuing rapid relief of the depressive symptoms of suicidal patients are discussed. Three case reports of monopolar depression and one case report for bipolar depression illustrate the routine and management of the patients. It is concluded that this method is safe, leads to a rapid relief of symptoms, and has fewer unpleasant side-effects. 1 reference.

002037 Blumenthal, Monica D. Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15261 **Depressive illness in old age: getting behind the mask.** *Geriatrics*. 35(4):34-37, 39, 43, 1980.

Symptoms of depression in old age, diagnostic considerations, and treatment are considered. In many old people, depressive illness presents symptoms similar to those commonly found in the young, while some older patients who suffer from depressive illness will appear in the doctor's office primarily complaining of some physical illness. In addition, some elderly patients developed depressive illnesses that appear to mimic dementias. Diagnostic considerations include the possibility that the depression may be drug-induced. A list of drugs that may produce depression is included. A second consideration in assessing the older patient with depressive illness is whether the depression is associated with a physical illness. There are a number of physical illnesses that appear to generate depressive symptoms. When the physician has ascertained that neither drug intoxication nor underlying disease is responsible for the depressive episode, pharmacologic treatment of the illness should be considered. As a rule, the tricyclic antidepressants are the drugs of choice. Side-effects of tricyclic antidepressants and effects of interactions with other drugs are indicated. 10 references.

002038 Bratfos, O.; Haug, J. O. Vestfold Sentralsykehus, 3100 Tonsberg, Norway **Comparison of sulpiride and chlorpromazine in psychoses: a double-blind multicentre study.** *Acta Psychiatrica Scandinavica*. 60(1):1-9, 1979.

In a material of 71 patients admitted because of acute or chronic psychoses, 32 were treated with sulpiride (up to 1,800mg per day) and 29 with chlorpromazine (up to 675mg). Duration of treatment was from 4 to 8 weeks. The effect of the 2 preparations was very similar as were the type and frequency of side-effects, except that sulpiride did not cause sun rash. 20 references. (Author abstract)

002039 Brogden, R. N.; Heel, R. C.; Speight, T. M.; Avery, G. S. no address **Mianserin: a new antidepressant.** *Current Therapeutics*. 20(4):23, 25, 28-29, 1979.

Pharmacokinetics, therapeutic efficacy, dosage, and side-effects of mianserin, a new antidepressant, are reviewed. Mianserin appears to be readily absorbed after oral administration, with peak plasma concentrations obtained 2 to 3 hours after ingestion, and a bioavailability of about 30%. Results of open and controlled trials in patients with depressive illness indicated that mianserin has antidepressant activity at doses of 30 to 120mg daily. Comparative studies have not found significant differences in therapeutic efficacy between mianserin and amitriptyline or imipramine. Mianserin also appears to have anxiolytic activity. Side-effects tend to be mild and disappear as treatment continues. They may include drowsiness. Anticholinergic side-effects seldom occur, and mianserin appears to be well tolerated by el-

derly and cardiovascular disease patients. Doses should be individualized, but usually the effective dose is 40 to 80mg daily.

002040 Busch, Daniel A.; Fang, Victor S.; Meltzer, Herbert Y. Meltzer, Dept. of Psychiatry, University of Chicago Pritzker School of Medicine, 950 East 59th St., Chicago, IL Serum prolactin levels following intramuscular chlorpromazine: two- and three-hour response as predictors of six-hour response. *Psychiatry Research*. 1(2):153-159, 1979.

To determine the time of true peak response to intramuscular (im) chlorpromazine (cpz), six male and four female psychiatric inpatients, who had not received neuroleptic medication for at least 1 week, received an injection of CPZ 25mg im; serum prolactin levels were monitored for 6 hours after injection. Peak serum prolactin levels occurred at 60 minutes in one subject, 90 minutes in three subjects, 120 minutes in two subjects, 180 minutes in three subjects, and 240 minutes in one subject. Area under the serum prolactin curve at 2 hours and area under the curve at 3 hours after CPZ injection were found to be good predictors of 6 hour area under the curve. Two hour studies should therefore not be considered inadequate; however, a 3 hour study length results in more precise characterization of prolactin response to im CPZ. 23 references. (Author abstract modified)

002041 Carman, John Scott; Wyatt, Richard Jed. Room 390, University Hospital, University Station, Birmingham, AL 35294 Calcium: pacesetting the periodic psychoses. *American Journal of Psychiatry*. 136(8):1035-1039, 1979.

The behavioral and biochemical effects of double-blind trials with psychotic patients using one agent that mimics and one that mitigates increases in serum calcium and phosphorus were studied. Dihydroxycholesterol (DHT) was given orally to eight psychotic patients. In each case marked increases in psychosis and agitation accompanied increases in serum calcium and phosphorus within two weeks after active drug was substituted for placebo. In the three patients whose psychoses exhibited periodic spontaneous exacerbations, the agitated episodes grew more severe. Serum creatine phosphokinase (CPK) increased in all but one patient. By contrast, when three periodically psychotic patients received synthetic salmon calcitonin (SCT), the severity and frequency of agitated episodes decreased while CSF calcium increased in all three. These data support the hypothesis that the observed abrupt increases in serum calcium and phosphorus might cause the opposite CSF calcium shifts, the behavioral agitation, and the increases in serum CPK frequently noted during acute psychosis. 19 references. (Author abstract)

002042 Chen, Char-Nie. Dept of Psychiatry, St. George's Hospital Medical School, Blackshaw Rd., London SW17 0QT, England Sleep, depression and antidepressants. *British Journal of Psychiatry*. 135(November):385-402, 1979.

The sleeping patterns of depressed patients and the effects of antidepressants on sleep are reviewed. Normal patterns of sleep are described, as well as the effect of different variables on normal sleep. Polygraphic sleep studies in depressed patients have shown that, in comparison with normal controls, they have difficulty in falling asleep, frequent shifts of sleep stages, increased time spent awake, early morning awakening, and a considerable reduction of stage four sleep. It is noted that many pharmacological agents are capable of suppressing REM sleep, and among them drugs that elevate mood are especially powerful. Antidepressive agents commonly used in current clinical practice include monamine oxidase inhibitors, tricyclics, tetracyclics, lithium, and electroconvulsive therapy; the effects of these agents on sleep are reviewed in depth. 227 references.

002043 Christodoulou, George N.; Madianos, Michael G.; Stefanis, Costas N.; Loukopoulou, Dimitris L. Eginition Hospital, 74 Vasilissis Sophias Ave., Athens, Greece Lithium prophylaxis in familial Mediterranean fever. *American Journal of Psychiatry*. 136(8):1082-1083, 1979.

A case study is reported in which a woman with familial Mediterranean fever (FMF) and related depression was given prophylactic lithium treatment. The lithium treatments reduced the number of FMF attacks and the severity of the few attacks she still had. In view of the patient's response to lithium, it is thought that the patient's FMF symptoms were somatic manifestations of an essentially endogenous depressive illness. 10 references.

002044 Cohen, Bruce M.; Miller, Alexander L.; Lipinski, Joseph F.; Pope, Harrison G. Mailman Research Center, 115 Mill St., Belmont, MA 02178 Lecithin in mania: a preliminary report. *American Journal of Psychiatry*. 137(2):242-243, 1980.

Tentative results from the treatment of manic patients with lecithin are reported. Eight newly admitted patients with manic-depressive illness, manic phase, were treated, and the results are consistent with a beneficial effect. These findings warrant controlled trials of lecithin, which is the dietary precursor of choline and which has been shown to increase choline and brain acetylcholine when given orally. 10 references.

002045 Colonna, L.; Petit, M.; Lepine, J. P. Service Hospitalo-Universitaire, Centre Hospitalier Specialise du Rouvray, F-76301 Sotteville les Rouen, France Bromocriptine in affective disorders: a pilot study. *Journal of Affective Disorders*. 1(3):173-177, 1979.

The use of bromocriptine in affective disorders was explored in 12 inpatients suffering from endogenous depression (9 bipolar, one schizoaffective and two unipolar patients) and three excited inpatients (two schizoaffective and one bipolar manic patient) who were treated for 15 days with doses of bromocriptine that varied between 10-15mg for depressed patients and 5-10mg for excited patients. At relatively low doses, bromocriptine appeared to be most effective in the patients exhibiting a manic or schizoaffective excitation. The response in the depressed patients was limited, with only three of 12 patients exhibiting a positive response. 15 references. (Author abstract modified)

002046 Daly, R. J.; Browne, P. J.; Morgan, E. Psychiatric Professional Unit, Cork Regional Hospital, Cork, Ireland Mianserin in the treatment of depressive illness: a comparison with amitriptyline. *Irish Journal of Medical Science*. 148(4):145-148, 1979.

In a double-blind comparative trial, 71 depressive inpatients were treated with either mianserin or amitriptyline for 3 weeks. The starting doses were 3 x 10mg daily of mianserin and 3 x 25mg daily of amitriptyline. The dose was then gradually increased to a possible maximum, depending on therapeutic response and side effects, of 80mg mianserin and 200mg amitriptyline daily. The response to treatment was assessed using the following rating scales before treatment and after 1, 2, and 3 weeks of treatment: the Hamilton Rating Scale for Depression, the Beck Self-Rating Scale for Depression, the Treatment Emergent Symptoms Scale, and a psychiatric Clinical Global Impression rating. Mianserin was found to be as effective as amitriptyline. No significant difference in side-effects was found between the two drugs. 17 references.

002047 Davidson, Jonathan; Raft, David; Freeman, Connie. John Umstead Hospital, Butner, NC 27509 Complementary effects of phenelzine and psychotherapy in long term treatment of depression. *Journal of Nervous and Mental Disease*. 167(10):632-634, 1979.

A case report is described wherein the monoamine oxidase (MAO) inhibitor phenelzine was administered for 10 months at different doses in combination with psychotherapy in the long-term treatment of depression. Drug treatment in the initial part of the study was double-blind. Weekly psychotherapy was instituted at the point of symptomatic recovery. At a reduced dose, in month 3, the patient experienced a relapse in depression. While platelet MAO inhibition was greater than 80% the patient was well, but at the point of relapse, inhibition was 14%. Clinical ratings at relapse (Beck and SCL-90 scales) revealed greater readiness by the patient to report psychological discomfort compared with the original interview. The combined effects of psychotherapy and pharmacotherapy were felt to be responsible for this change. However, psychotherapy in this form and duration did not prevent relapse, which depended upon maintaining an adequate dose of phenelzine. 11 references. (Author abstract modified)

002048 Degkwitz, R.; Koufen, H.; Consbruch, U.; Becker, W.; Knauf, H. Koufen: Universitäts-Nervenklinik, Hauptstrasse 5, D-7800 Freiburg i. Br., Germany / **Lithium balance studies during mania./ Untersuchungen zur Lithiumbilanz während der Manie.** *International Pharmacopsychiatry.* 14(4):199-212, 1979.

Lithium balance studies were conducted in 19 manic and 6 depressed patients and it was found that: 1) the mean daily lithium requirement for manics was 52mM and 30mM for depressed Ss; 2) renal elimination after optimal blood lithium levels had been reached was 76% in manics and 97% in depressed Ss; 3) an unchanged lithium half-life time occurred in mania; 4) in both groups, no significant differences in lithium and creatinine clearance were noted; 5) standard diet or unrestricted sodium chloride administration did not significantly influence the lithium requirement or lithium retention. After exclusion of a renal or dietetic cause for increased lithium requirement or retention during mania, the existence of a lithium pool dependent on the presence of a manic psychosis seems probable and somatic influences on endogenous psychosis should be considered. 41 references. (Journal abstract modified)

002049 DiMascio, Alberto; Weissman, Myrna M.; Prusoff, Brigitte A.; Neu, Carlos; Zwilling, Maggie; Klerman, Gerald L. Weissman: Depression Research Unit, Connecticut Mental Health Center, Suite 2A, 904 Howard Avenue, New Haven, CT 06519 **Differential symptom reduction by drugs and psychotherapy in acute depression.** *Archives of General Psychiatry.* 36(13):1450-1456, 1979.

The combination of amitriptyline hydrochloride and short-term interpersonal psychotherapy, each treatment alone, and no treatment control condition were compared in the treatment of an ambulatory acute nonbipolar, nonpsychotic depressive sample. Results show the efficacy of both psychotherapy and amitriptyline in overall symptom reduction. Amitriptyline and psychotherapy were about equal, and the effects of both treatments in combination were additive. The additive effect of combined treatment was largely due to the differential effects of the two treatments. Amitriptyline had its effect mainly on the vegetative symptoms of depression such as sleep and appetite disturbance, these occurred early in treatment, often within the first week. Psychotherapy had its effect mainly on mood, suicidal ideation, work, and interests; these effects occurred slightly later, at 4 to 8 weeks. 25 references. (Author abstract)

002050 Elsass, Peter; Møllerup, Erling T.; Rafaelsen, Ole J.; Theilgaard, Alice Dept. of Psychiatry, Rigshospitalet 9, Blegdamsvej, DK-2100, Copenhagen Ø, Denmark **Lithium effects on time estimation and mood in manic-melancholic patients: a study of diurnal variations.** *Acta Psychiatrica Scandinavica.* 60(3):263-271, 1979.

Psychological effects of lithium treatment emphasizing the importance of diurnal variations were evaluated. Subjects included a group of lithium treated patients, a group of psychiatric patients not given lithium, and an untreated group of healthy subjects. In all groups the internal clock was slower in the morning than in the night. The results indicate that the internal clock in lithium treated patients was slower than in the two other groups, but only at night. Mood variations from night to morning were observed in all three groups. The group of lithium treated patients had fewer complaints as to self-report of mood variations compared with the other groups. 17 references. (Author abstract modified)

002051 Elwan, O. Cairo University, Cairo, Egypt **A comparative study of viloxazine and imipramine in the treatment of depressive states.** *Journal of International Medical Research.* 8(1):7-17, 1980.

The therapeutic efficacy and clinical profile of viloxazine in the treatment of depressive states was investigated and compared with that of imipramine, a widely used tricyclic antidepressant drug. The pattern of antidepressant activity of viloxazine appears similar to that of imipramine. Both register improvement in depression and eight other target symptoms, according to the Hamilton Rating Scale for Depression. Viloxazine appears superior in its energizing action, as well as in relieving somatic anxiety and hypochondriasis and in its drive stimulating properties. In view of the balanced profile of action and minimal tolerable side-effects, viloxazine might be recommended for treating all types of depression. 13 references.

002052 Elwan, O.; Adam, H. K. Adam: Safety of Medicines Dept., ICI Pharmaceuticals Division, Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG, England **Relationship between blood and cerebrospinal levels of the antidepressant agent viloxazine.** *European Journal of Clinical Pharmacology.* 17(3):179-182, 1980.

The relationship between blood and cerebrospinal fluid (CSF) levels of the antidepressant agent viloxazine was investigated following acute and chronic dosing in depressed patients. Blood profiles confirm previous findings that viloxazine is rapidly absorbed and eliminated with a half life of 4.5 hours. Viloxazine crosses the blood/brain barrier and concentrations in CSF remain virtually unchanged over a 10 hour period postadministration. Viloxazine does not accumulate in CSF on chronic administration. The fact that CSF levels do not reflect concentrations in blood has significant implications on any attempt to correlate the clinical efficacy and the pharmacokinetic behavior of an antidepressant agent. 16 references. (Author abstract)

002053 Exteine, Irl; Pottash, A. L. C.; Gold, Mark S.; Cadet, Jean; Sweeney, Donald R.; Davies, Robert K.; Martin, David M. Fair Oaks Hospital, 19 Prospect St., Summit, NJ 07901 **The thyroid-stimulating hormone response to thyrotropin-releasing hormone in mania and bipolar depression.** *Psychiatry Research.* 2(2):199-204, 1980.

Thyroid stimulating hormone (TSH) response to thyrotropin-releasing hormone (TRH) was studied in manic and bipolar depressed patients. The release of TSH from the pituitary after infusion of 500mcg of TRH was decreased in manic patients and increased in bipolar depressed patients compared to a control group of patients with personality disorders. Results suggest that the TRH test may be useful in the diagnosis of psychiatric disorders and in the prediction of response to pharmacotherapy. The role of central monoaminergic systems in change in the TSH response to TRH is discussed. 14 references. (Author abstract modified)

002054 Fieve, Ronald R. Foundation for Depression and Manic Depression, 7 East 67th Street, New York, NY 10021 **The clinical effects of lithium treatment.** Trends in Neurosciences. 2(3):66-68, 1979.

Clinical experience with lithium is reviewed. Lithium is given as lithium carbonate in tablet or capsule form usually by outpatient clinics which monitor the patients' mood swings and blood levels. Some of the side-effects which are present initially but later disappear include nausea, fatigue, muscle weakness, fine hand tremor, and drowsiness. The various theories which attempt to explain how lithium works in depressive and manic depressive patients are considered. The behavioral effects of lithium are compared with those of the major tranquilizers. 7 references.

002055 Fink, Max. Dept. of Psychiatry and Behavioral Science, SUNY at Stony Brook, New York, NY **Mianserin -- a new tetracyclic antidepressant.** Psychopharmacology Bulletin. 15(3):27-29, 1979.

Clinical studies of the antidepressant effects of mianserin are reviewed. Mianserin exerts potent antidepressant effects at daily doses of 40 to 80mg. It has sedative qualities and a long duration of action permitting a single bedtime dose. It penetrates the CNS rapidly and has no toxic cardiovascular or anticholinergic effects. 3 references.

002056 Fink, Max. Dept. of Psychiatry and Behavioral Science, School of Medicine, SUNY, Stony Brook, NY 11794 **A neuroendocrine theory of convulsive therapy.** Trends in Neurosciences. 3(1):25-27, 1980.

A neuroendocrine theory of the mechanisms of action of convulsive therapy (including chemically-induced convulsive therapy and electroconvulsive therapy -- ECT) is proposed. It is hypothesized that the antidepressant efficacy of convulsive therapy results from the increased release and more widespread distribution of peptides with behavioral effects. It is noted that repeated and spaced induction of seizures relieves the symptoms of severe depressive mood disorders, that bilateral seizures are evidence of brainstem stimulation, and that vegetative symptoms are favorable predictors of convulsive therapy outcome. Two recent lines of evidence in studies of depression are cited in support of the neuroendocrine hypothesis: patients with severe depression demonstrate neuroendocrine abnormalities, and these functions return to normal with ECT. Some peptides, which originate, or are found in high concentrations, in hypothalamic structures, have both behavioral (extraendocrine) effects and diffuse cerebral distributions. 14 references. (Author abstract modified)

002057 Garfinkel, Paul E.; Brown, Gregory M.; Warsh, Jerry J.; Stancer, Harvey C. Dept. of Psychiatry, University of Toronto, Toronto, Ontario, Canada **Neuroendocrine responses to carbidoa in primary affective disorders.** Psychoneuroendocrinology. 4(1):13-20, 1979.

Levels of growth hormone, prolactin, thyroid stimulating hormone (TSH), and cortisol were determined in 18 patients with primary affective disorders (11 bipolar and 7 unipolar) and in 10 normal controls treated with carbidoa (100mg, three times a day for 7 days). Bipolar depressed females failed to show the prolactin elevation normally observed in response to carbidoa, and their levels of carbidoa were significantly lower than controls. Bipolar depressed women also had higher levels of plasma TSH than controls. No differences between depressed and normal Ss were evident in males. Results support the concept of altered neurotransmitter activity in some patients with primary affective disorders. 49 references. (Author abstract modified)

002058 Gayral, L.-F.; Escande, M.; Goldberger, E. Clinique de Psychiatrie, Faculte de Medecine, Purpan, C.H.U., F-31052 Toulouse Cedex, France **Combination of reserpine with lithium in the treatment of manic dysthymias resistant to lithium.** Association de la reserpine au lithium pour le traitement de dysthymies maniaques lithio-resistances. Annales Medico-Psychologiques. 137(5):506-516, 1979.

The effects of reserpine in combination with lithium on eight patients suffering from manic dysthymias were studied. Results are tabulated in categories by sex, age at the beginning of treatment with reserpine, clinical forms (various forms of cyclothymia and manic dysthymia), length of previous treatment with lithium, reason for treatment with reserpine, length of observation of the treatment with reserpine, average and maximum dosage of reserpine, tolerance and incidents, and results such as good results in five cases, average result in one case, half failure in one case, and failure in one case. A discussion follows the text of the article.

002059 German, G. Allen; Stampfer, H. G. Dept. of Psychiatry, University of Western Australia, Perth 6009, Western Australia, Australia **Hypothalamic releasing factor for reactive depression.** Lancet. No. 8146:789, 1979.

The effects of hypothalamic releasing factor (HRF) on 27 patients exhibiting symptoms of depression are reported. HRF had little or not effect on patients with primary affective illness. One patient with bipolar disturbance swung from severe depression to hypomania. In the eight patients with stress associated depression, HRF was effective. Depressive symptoms resolved and feelings of normal functioning with normal coping were restored. HRF also improved sleep patterns in all patients. Two case histories are reported which illustrate the beneficial effects of HRF in cases of depression where prolonged stress and exhaustion have played a role.

002060 Gillin, J. Christian; Sitaram, N. NIMH, Bethesda, MD 20205 **Acetylcholine and norepinephrine: sleep and mood. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 1 p.

The latency to REM sleep following arecoline (administered 25 minutes following the first REM period) was measured in unmedicated, remitted patients with primary affective illness and in controls to test the hypothesis that underlying cholinergic mechanisms might be involved in affective illness. The data indicate that REM latency is shortened by pharmacological treatments which enhance cholinergic neurotransmission and block catecholamine synthesis. These results appear to be consistent with the neurophysiological model of Hobson and McCarly, to be relevant to the understanding of the disturbances of sleep observed in depression, and to offer new pharmacological strategies for the study of primary illness in remission. (Author abstract modified)

002061 Gold, Philip W.; Weingartner, Herbert; Ballenger, James C.; Goodwin, Frederick K.; Post, Robert M. Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **Effects of l-desamino-8-arginine vasopressin on behaviour and cognition in primary affective disorder.** Lancet. No. 8150:992-994, 1979.

Behavioral and cognitive effects of l-desamino-8-d-arginine vasopressin (DDAVP), a synthetic analogue of vasopressin with prolonged half-life and antidiuretic and low pressor activity, were examined in a double-blind placebo controlled trial in four patients with major affective illness. Three of the four patients showed highly significant and consistent improvements in tests designed to measure the formation, coding, and organization of long-term trace events in memory. Two patients also showed significant but less consistent amelioration of other depressive

symptoms during DDAVP treatment. Findings implicate central vasopressin function in the processing of information and possibly in other aspects of affective illness. 10 references. (Author abstract)

002062 Goodnick, Paul J.; Meltzer, Herbert L.; Dunner, David, L.; Fieve, Ronald R. Dept. of Psychiatry, Veterans Administration Hospital, Mount Sinai School of Medicine, 130 W. Kingsbridge Rd., Bronx, NY 10468 **Repression and reactivation of lithium efflux from erythrocytes.** *Psychiatry Research.* 1(2):147-152, 1979.

Efflux of lithium from human erythrocytes was studied in patients before, during, and after discontinuation of administration of lithium carbonate. Onset of lithium-induced repression of efflux took approximately 10 days and was significantly shorter in patients who had had lithium therapy previously. Reactivation took a longer period of time (approximately 2 weeks) and was found to be related to duration of lithium therapy. Theoretical pathways of lithium flow through membranes are discussed. 19 references. (Author abstract)

002063 Itil, Turan M.; Michael, Stanley T.; Soldatos, Constantine. Dept. of Psychiatry, New York Medical College, New York, NY **Androgens as antidepressants.** *Psychopharmacology Bulletin.* 15(3):31-33, 1979.

Studies of the antidepressant effects of mesterolone, a synthetic androgen, are summarized. The drug produced significant changes in human EEG profiles; the effects of low doses (1 and 10mg) were similar to those of psychostimulants, while the effects of high doses (100 to 1600mg) resembled those of tricyclic antidepressants. A significant improvement in depressive symptomatology was seen in moderately to severely depressed outpatients treated with mesterolone, but placebo treated patients also showed significant improvement in the same study. Plasma testosterone levels, protein bound testosterone levels, and luteinizing hormone levels were significantly reduced in the mesterolone patients, compared to the placebo group. No significant side-effects were observed during mesterolone treatment in daily doses up to 450mg for up to 6 months. 9 references.

002064 Katanec, Nada. Dept. of Psychiatry, University Hospital Centre, Zagreb, Yugoslavia **Organization of nonhospital treatment of acute depressive conditions and results of therapy with Noveril.** *Organizacija izvanbolničkog liječenja akutnih depresivnih stanja uz prikaz rezultata liječenja Noverilom.* *Socijalna Psihijatrija.* 7(1):87-95, 1979.

A group of 34 patients were treated for acute depressive disorders. Certain variables from their life (chronic frustrations and acute conflicts), and results of the treatment with the antidepressant drug dibenzepine (Noveril) are discussed. Among chronic frustrations observed, disturbed marital relations, chronic organic diseases, and the loss of one or both parents before the age of 12 were encountered most frequently. Among current conflicts acting as provocative factors, those relating to failure in one's work, adultery, material losses, and the death of a near person appeared to be the most important ones. The assessment of the effect of dibenzepine after a 3 week application and the follow-up of the patient during this treatment have shown that the results are very good and that the use of the preparation in non-hospital psychiatric practice is well grounded. Antidepressive therapy should be built upon a careful exploration and assessment of provocative factors, collaboration with the patient's relatives and friends, collaboration with his working environment, frequent followup examinations, contact with the respective general practitioner, use of public nursing, and choice of antidepressive preparations. 16 references. (Journal abstract modified)

002065 Keith, David V. Dept. of Psychiatry, University of Wisconsin Center for Health Sciences, Madison, WI 53792 **Family therapy and lithium deficiency.** *Journal of Marital and Family Therapy.* 6(1):49-53, 1980.

The possibility that lithium carbonate's usefulness in relieving the more dramatic symptoms of bipolar affective disorder may obscure family systems components of this illness is discussed in the context of the infantilization of the patient, which is a concomitant of lithium therapy. It is contended that a compromised form of family therapy often results during lithium treatment of a family member, and that this compromised therapy may stabilize the marriage but cause troubles for the larger family system. A partial modus operandi for keeping family therapy systems oriented and avoiding the infantilization of the identified patient which occurs when the importance of purely medical treatment is overplayed is presented. 6 references. (Author abstract modified)

002066 Kellams, Jeffrey J.; Klapper, Marietta H.; Small, Joyce G. LaRue D. Carter Memorial Hospital, 1315 West 10th St., Indianapolis, IN 46202 **Trazodone, a new antidepressant: efficacy and safety in endogenous depression.** *Journal of Clinical Psychiatry.* 40(9):390-395, 1979.

The effectiveness of trazodone was assessed over a 4 week period under double-blind conditions. Twenty-eight inpatients with a diagnosis of endogenous depression received either trazodone, imipramine, or placebo. Trazodone was significantly better than placebo and frequently better than imipramine according to analyses of the results of the Hamilton Psychiatric Scale for Depression, severity of illness and clinical global improvement ratings, and the Global Ward Behavior Scale. Significant improvement was reported in the trazodone group by the end of the first week of therapy, particularly in those symptoms associated with depression and accompanying anxiety. Fewer side-effects were reported with trazodone than with imipramine. 17 references. (Author abstract)

002067 Kielholz, P. Psychiatrische Universitätsklinik, Wilhelm-Klein-Strasse, 27, CH-4000 Basel, Switzerland **The classification of depressions and the activity profile of the antidepressants.** *Progress in Neuro-Psychopharmacology.* 3(1-3):59-63, 1979.

The classification of depressive illnesses is discussed, and activity profiles of various antidepressant drugs are described. It is contended that a prerequisite for the successful treatment of depression is an accurate diagnosis. The nosological classification proposed by the World Health Organization's International Classification of Diseases distinguishes three main groups of depressive states (somatogenic, endogenous, and psychogenic depressions). In the somatogenic depressions, the organic aspects of the depression must be treated before the depression can be alleviated. In endogenous and psychogenic depressions, the diagnosis determines the choice of antidepressant drugs. 4 references. (Author abstract modified)

002068 Kielholz, P.; Terzani, S.; Gastpar, M. University Psychiatric Clinic, Basel, Switzerland **Treatment for therapy resistant depressions.** *International Pharmacopsychiatry.* 14(2):94-100, 1979.

Recommended approaches to treating therapy resistant depression are examined, with emphasis on developments over the past 7 years toward employing intensive courses of treatment with a major tranquilizer given in combination with an antidepressant. This approach replaces the treatment of refractory cases with combined antidepressant and electroconvulsive therapies. The mode of action of the therapeutic agents is described and observations of their effectiveness in counteracting endog-

enous and psychogenic depressions are briefly reported. 18 references.

002069 Kirkegaard, C.; Bjorum, N. Medical Dept. E., Frederiksberg Hospital, DK-2000 Copenhagen F, Denmark **TSH responses to TRH in endogenous depression.** *Lancet*. No. 8160:152, 1980.

In a letter to the editor, thyroid stimulating hormone (TSH) responses to thyrotropin releasing hormone (TRH) in endogenous depression are discussed. Results from an experiment with 34 patients support the idea that in the individual patient with endogenous depression, regardless of the polarity, TSH is impaired during depression or when antidepressive treatment has only a symptomatic effect, and that the response returns to normal when the patient is cured and does not need further treatment. The impaired TSH response to TRH may reflect an underlying neuroendocrine disorder. It is suggested that long-term treatment with tricyclic antidepressants can be safely stopped when TSH increases, and that this may be a reliable biochemical index for the evaluation of the curative effect of different antidepressive treatments. 2 references.

002070 Klicpera, C.; Albert, W.; Strian, F. Max-Planck-Institut für Psychiatrie, Kraepelinstrasse 10, D-8000 Munich 40, Germany **Effects of somatic treatments on mood in endogenous depression.** *Acta Psychiatrica Scandinavica*. 60(2):129-136, 1979.

The effects of ECT, amitriptyline, clomipramine, maprotiline and desipramine on the course of endogenous depression were compared. Patients (n=105) were administered repeated self-administered mood questionnaires as the outcome measure. Remission was more rapid after ECT therapy than psychopharmacological treatment, but the absolute improvement did not differ significantly between ECT and other somatic therapies. Improvement in response to clomipramine was more rapid than to other psychopharmacological agents, and did not differ from that in response to ECT. The advantages and disadvantages of ECT for endogenous depression are discussed. 15 references. (Author abstract)

002071 Langer, Gerhard; Schonbeck, George; Koinig, Greta; Lesch, Otto; Schussler, Margot; Waldhauss, Werner. Dept. of Psychiatry, University of Vienna, A-1097 Vienna, Austria **Antidepressant drugs and the hypothalamic-pituitary-thyroid axis.** *Lancet*. No. 8159:100-101, 1980.

The role of the hypothalamic/pituitary/thyroid axis in antidepressant drug effects, examined in 21 unipolar depressed women treated with clomipramine, is reported. TSH response to TRH was studied at admission, after 2 and 4 weeks intravenous clomipramine, and during the outpatient phase on oral clomipramine. Considerable or complete improvement in the patient's condition was found to be significantly associated with a positive trend of the TSH response, while poor or no improvement was more frequently associated with a negative trend. In patients relapsing within a year despite continuous clomipramine treatment, during improvement peak TSH responses increased whereas at relapse peak TSH response decreased. Findings suggest that the hypothalamic/pituitary/thyroid axis may be involved in the therapeutic effects of tricyclic antidepressants.

002072 Lerner, Yakov; Lwow, Etan; Levitin, Aryeh; Belmaker, Robert H. Belmaker: Jerusalem Mental Health Center-Ezrath Nashim, POB 140, Jerusalem, Israel **Acute high-dose parenteral haloperidol treatment of psychosis.** *American Journal of Psychiatry*. 136(8):1061-1064, 1979.

In order to determine if high dose parenteral haloperidol can specifically and rapidly reverse psychotic thought disorders, 20 newly admitted psychotic patients received 20-35mg of haloperi-

dol intravenously and 20 patients received 30-40mg of diazepam intravenously. Posttreatment ratings at four and 24 hours with the Brief Psychiatric Ratings Scale and the Clinical Global Impressions revealed significant improvement in both groups, but no significant differences between the two treatments. 18 references. (Author abstract)

002073 Levine, Ruth R. Division of Medical and Dental Sciences, Boston University School of Medicine, 80 East Concord Street, Boston, MA 02118 **The role of plasma concentrations in the use of tricyclic antidepressant drugs.** *Progress in Neuro-Psychopharmacology*. 3(1-3):211-222, 1979.

The role of plasma concentrations in the use of tricyclic antidepressant drugs is evaluated, and the superiority of sound clinical judgment and dosage adjustment for individual patients over mere plasma level determinations is affirmed. The range of tricyclic antidepressant plasma levels needed for therapeutic response remains largely unresolved, since dose response relationships have not yet been clearly defined for either therapeutic or nontherapeutic effects. The fact that certain patients apparently become more depressed at higher plasma levels must be balanced against the facts that depression is a mixture of disorders as yet poorly distinguishable and that tricyclic antidepressants have multiple pharmacologic effects. It is contended that there is presently no justification for routinely monitoring tricyclic antidepressant plasma levels. 25 references. (Author abstract modified)

002074 Lindberg, D.; Ahlfors, U. G.; Dencker, S. J.; Fruensgaard, K.; Hansten, S.; Jensen, K.; Ose, E.; Pihkanen, T. A. Department II, Lillhang Mental Hospital, Box 3005, S-422 03 Hisingen Backa 3, Sweden **Symptom reduction in depression after treatment with L-tryptophan or imipramine: item analysis of Hamilton Rating Scale for depression.** *Acta Psychiatrica Scandinavica*. 60(3):287-294, 1979.

The analysis of changes in separate items of the Hamilton depression scale (HRS) in patients treated with either L-tryptophan or imipramine is presented. Item analysis of HRS, before the investigation and weekly during the trial period, demonstrated few statistically different mean scores on individual items between the two treatment groups. After 3 weeks of treatment a statistically significant item mean reduction was found in the item Agitation in favor of imipramine treated, and in the item Work and Activities in favor of L-tryptophan treated endogenously depressed patients. After 3 weeks of treatment a statistically significant item mean reduction on the 5% level was found in the item Suicide in favor of imipramine treated nonendogenously depressed patients. Results show that, after 3 weeks of treatment, imipramine and L-tryptophan has decreased the mean score on individual items of HRS in about the same degree. 8 references. (Author abstract modified)

002075 Maany, Iradj; Mendels, Joseph; Frazer, Alan; Brunswick, David. Veterans Administration Hospital (151E), University and Woodland Avenues, Philadelphia, PA 19104 **A study of growth hormone release in depression.** *Neuropsychobiology*. 5(5):282-289, 1979.

Human growth hormone response to apomorphine and levodopa were studied in five groups: normal men aged 28 to 58 years, unipolar depressed men aged 28 to 64 years, bipolar I depressed men aged 30 to 56 years, bipolar II depressed men aged 32 to 64, and secondary or reactive depressed men aged 30 to 53 years. Apomorphine and levodopa are known to stimulate growth hormone release via a dopaminergic pathway in median eminence. Findings did not indicate any significant abnormality in the dopaminergic systems of the groups with affective disorders. Due to variability in the peripheral metabolism of levo-

dopa, and the complexity of growth hormone release, it is noted that conclusive findings from any study involving only one neurotransmitter system is not possible. 26 references. (Author abstract modified)

002076 Man, Pang L. Northville Regional Psychiatric Hospital, 41001 Seven Mile Road, Northville, MI 48167 **Correlation of saliva and serum lithium.** *Psychosomatics*. 20(11):758-759, 1979.

Lithium carbonate levels of 90 blood samples and 180 saliva samples from 30 manic-depressive patients receiving lithium carbonate treatment were measured. The Pearson correlation coefficient and the mean ratio of saliva to serum lithium carbonate levels was 2.16. Saliva levels of lithium carbonate ranged from 1.29 to 3.24 mEq/liter, equivalent to serum lithium levels of 0.6 to 1.5 mEq/Liter. The use of commercially available sour chewing gum proved a more effective and convenient way to collect saliva than the current existing procedure. Saliva levels of lithium carbonate appeared to correlate well with serum levels, and were much easier to obtain. 8 references. (Author abstract)

002077 Mann, John; Gershon, Samuel. Neuropsychopharmacology Research Unit, Dept. of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **L-deprenyl, a selective monoamine oxidase type-B inhibitor in endogenous depression.** *Life Sciences*. 26(11):877-882, 1980.

A clinical trial of L-deprenyl, a selective monoamine oxidase (MAO) type-B inhibitor, in treatment of endogenous depression is described. In a group of 12 endogenously depressed patients who failed to respond to a week of placebo medication, L-deprenyl produced a significant improvement over the whole range of depressive symptomatology. This is the first reported study of the antidepressant properties of L-deprenyl using a lower dose range, where both selective inhibition of type-B MAO would occur and the patient would be protected from the hypertensive cheese reaction. The possibility of an MAO inhibitor relatively free from the risk of a cheese reaction and yet an effective antidepressant would be a valuable new therapeutic agent. In addition, monitoring the degree of inhibition of platelet MAO may be a useful way of determining the therapeutic dosage for individual patients. 23 references. (Author abstract modified)

002078 McClelland, H. A.; Kerr, T. A.; Stephens, D. A.; Howell, R. W. Dept. of Psychiatry, St. Nicholas Hospital, Gosforth, Newcastle upon Tyne NE3 3XT, England **The comparative antidepressant value of lofepramine and amitriptyline: results of a controlled trial with comments on the scales used.** *Acta Psychiatrica Scandinavica*. 60(2):190-198, 1979.

A double-blind controlled trial comparing the antidepressant activity of amitriptyline with lofepramine is reported. Analysis of the Hamilton Depression Rating Scale scores at the beginning and end of the trial showed no significant difference between the therapeutic efficacy of lofepramine and amitriptyline. However, patients with endogenous depression responded significantly more rapidly to lofepramine as measured by Visual Analogue Scales and showed a significantly greater degree of clinical improvement after 4 weeks of treatment, as measured by Global Assessment. Adverse effects were similar in the two treatment groups. The use of rating scales in trials of depressive illnesses is discussed. The Visual Analogue Scale for depression was found to be a simple, useful and valid measure. 10 references. (Author abstract modified)

002079 Møllerup, E. T.; Dam, H.; Wildschiodtz, G.; Rafaelsen, O. J. Psychochemistry Institute, Rigshospitalet 9, Blegdamsvej, DK-2100 Copenhagen O, Denmark **Lithium effects: relation to**

lithium dose and to plasma peak levels. *Acta Psychiatrica Scandinavica*. 60(2):177-184, 1979.

In a 24 hour study, plasma peak lithium was determined in manic melancholic patients who routinely had their entire lithium dose at night. A correlation analysis was undertaken of the relation of plasma peak level and the dose of lithium to a number of lithium-induced changes: increase in urine volume, weight gain, decrease in plasma phosphate, increase in plasma magnesium, decrease in plasma urea, increase in plasma alkaline phosphatase, increase in urinary pH. Only the changes in plasma phosphate and in urine pH were significantly correlated to the peak value of plasma lithium. The increase in urine volume was significantly correlated to the dose of lithium. 16 references. (Author abstract)

002080 Mendlewicz, J.; Linkowski, P.; Rees, J. A. Erasme Hospital, University of Brussels, Route de Lennik, 808, 1070 Brussels, Belgium **A double-blind comparison of dothiepin and amitriptyline in patients with primary affective disorder: serum levels and clinical response.** *British Journal of Psychiatry*. 136(February):154-160, 1980.

In a double-blind parallel group study, 32 patients suffering from a primary affective disorder received either dothiepin or amitriptyline. Serum concentrations of total dothiepin plus nortriaden or amitriptyline and nortriptyline were estimated. A similar therapeutic response was seen with both drugs but there was no correlation with serum concentrations of amitriptyline or nortriptyline, whereas serum dothiepin correlated positively with clinical response. 20 references. (Author abstract)

002081 Michalik, Michael; Uebelhack, Ralf; Seidel, Karl; Ehle, Giesela; Grote, Ilona. Bereich Medizin (Charité) der Humboldt-Universität, Schumannstrasse 20/21, DDR-104 Berlin, Germany **The behavior of vegetative parameters under administration of Ouabain (g-Strophanthin) in endogenous depressed patients./ Das Verhalten vegetativer Parameter unter Anwendung von Ouabain (g-Strophanthin) bei endogen depressiven Patienten.** *Schweizer Archiv für Neurologie, Neurochirurgie, und Psychiatrie*. 125(1):163-170, 1979.

To examine the salivation rate of endogenous depressive patients, the salivation rate of 7 normal controls and 17 endogenous depressive patients was measured, via the Strongin-Hinsie-Peck test. The salivation rate of controls was constant. The endogenous depressive patients developed a diminishing of depression depth under treatment with Ouabain (g-Strophanthin) between the 6th and 12th day, which was associated with reduction of the drive diminishing and the restoration of mood. The effective salivation rate gained during treatment. Possible principles of the influence of Ouabain are discussed. (Journal abstract modified)

002082 Minter, Richard E.; Mandel, Michel R. Dept. of Psychiatry, University Medical Center, 1405 East Ann Street, Ann Arbor, MI 48109 **The treatment of psychotic major depressive disorder with drugs and electroconvulsive therapy.** *Journal of Nervous and Mental Disease*. 167(12):726-733, 1979.

Medical records of 54 patients demonstrating research diagnostic criteria for psychotic major affective disorder (depression with psychotic symptoms) were reviewed to evaluate the efficacy of tricyclic antidepressants alone, antipsychotics, the two in combination, or electroconvulsive therapy (ECT). Antidepressants alone were found to be ineffective or only partially effective in treating psychotic depression unless somatic or depressive delusions were the only psychotic symptoms. Antipsychotics alone were usually effective in providing at least a partial response, particularly with psychotic symptoms. Excellent responses of the depressive and psychotic elements were provided

with ECT, ECT with antipsychotic medication, and the combination of antidepressant and antipsychotic medications. These latter treatments may be the most appropriate for depression with psychotic features. 53 references. (Author abstract modified)

002083 Molnar, G.; Wallace, J.; Gupta, R. Dept. of Psychiatry, McMaster University, Hamilton, Ontario, Canada **Guidelines for clinical use in interpreting tricyclic plasma levels.** Canadian Journal of Psychiatry. 24(6):532-536, 1979.

Guidelines for the clinical interpretation of tricyclic plasma levels are presented using data obtained from studies of plasma concentrations of amitriptyline and other major antidepressants and their active metabolites in over 300 patients. It is contended that in an individual patient it is useful to make treatment decisions based on the changes in relations between dose/plasma level/clinical state. Knowledge of plasma levels can be used according to the suggested guidelines for adjustment of a drug regimen to obtain therapeutic levels. 16 references.

002084 Natale, Michael. Dept. of Psychology, University of Pennsylvania, 3815 Walnut Street, Philadelphia, PA 19174 **The relationship of imipramine plasma levels and verbalized hostility in nondelusional endogenous depressives.** Journal of Nervous and Mental Disease. 167(10):620-625, 1979.

The relationship of imipramine plasma levels and verbalized hostility in eight nondelusional endogenous depressive patients was examined using the Gotteschalk verbal sample technique. Hostility directed inward and outward was measured following imipramine in placebo, subclinical, and clinical doses. Hostility out was found to increase significantly only when patients obtained plasma levels of imipramine considered to be clinically effective. Hostility in was unrelated to imipramine, but a nonsignificant trend of lowered anxiety was found for both subclinical and clinical plasma levels of imipramine. All of the changes in verbalized affect were observed within a postdrug period which predated overt clinical change. Hence, the relationship of subclinical and clinical plasma levels of imipramine to verbalized affect was considered to serve as a behavioral index of clinically effective plasma levels of imipramine which could be predictive of favorable outcome. 21 references. (Author abstract modified)

002085 Nielsen, Johan Lanng. Medicinsk-haematologisk afdeling, Aarhus Amtssygehus, DK-8000 Aarhus C, Denmark **ECG changes during treatment with nortriptyline in a once-a-day dosage.** Neuropsychobiology. 6(1):48-51, 1980.

In 21 patients suffering from endogenous depression and given nortriptyline 150mg per day for 4 weeks in a once a day dosage, an electrocardiographic study was made with electrocardiogram recordings at different times during the treatment. At the same time the plasma concentration of nortriptyline was determined. During the treatment the heart rate increased significantly, both at the minimum and the maximum concentration of nortriptyline. At the maximum concentration the PQ interval increased significantly. None of the patients developed an A-V block, though three patients did develop extrasystoles. None of the patients had severe subjective symptoms and they all finished the trial as planned. There was no correlation between the plasma concentration of nortriptyline and the increase in heart rate. The trial revealed no serious cardiac influence during treatment with nortriptyline in a once a day dosage. 7 references. (Author abstract)

002086 Nielsen, Johan Lanng. Medicinsk-haematologisk afdeling, Aarhus Amtssygehus, DK-8000 Aarhus C, Denmark **Plasma prolactin during treatment with nortriptyline.** Neuropsychobiology. 6(1):52-55, 1980.

The plasma concentrations of prolactin and nortriptyline were determined in 17 patients with endogenous depression treated for 4 weeks with nortriptyline once a day. None of the patients developed galactorrhea. A moderate but statistically significant increase (about 25%) in the plasma prolactin was found after 3 weeks of treatment. There was no correlation between the plasma levels of prolactin and of nortriptyline. The results indicate that nortriptyline does not belong to the group of psychotropics which produce considerable increases in the plasma concentration of prolactin. 11 references. (Author abstract)

002087 no author. no address **An interview with Leo E. Hollister, MD, on: using psychopharmacology more effectively.** Behavioral Medicine. 6(11):24-29, 1979.

Strategies which physicians should consider in treating depression secondary to somatic illness are examined in an interview with Dr. Leo E. Hollister. Views on the polypharmacologic approach in treating affective disorders, the potential addictive abuse of alcohol and benzodiazepines, and the clinical implications for the new generation of antidepressants are presented. The controversy surrounding the biogenic amine hypothesis for the etiology of depression is also addressed. It appears that the newer tetracyclic and bicyclic antidepressants currently being used in Europe are challenging the supremacy of the tricyclic antidepressants.

002088 No author. no address **Urinary MHPG: improved tricyclic antidepressant drug selection in clinical practice.** Medical Journal of Australia. 2(5):233-234, 1979.

The utility of urinary 3-methoxy-4-hydroxy-phenyl-ethylene-glycol (MHPG) as a guide to the selection of optimal antidepressants was explored. MHPG is the main metabolite of noradrenaline. Depressed patients with low urinary MHPG have been found to respond to drugs that enhance noradrenaline activity. A study is reported in which 24-hour urinary MHPG levels were used as predictors of patients' responses to specific tricyclic antidepressants. It was found that the patients with low or high urinary MHPG levels responded better to the tricyclic antidepressant therapy than did the comparison group. It was concluded that the 24 hour MHPG output provides a valid chemical basis for individual antidepressant drug selection. 2 references.

002089 no author. H. E. Lehmann: Dept. of Psychiatry, McGill University, Montreal, Quebec, Canada **Canadian colloquium on response to antidepressants - abridged proceedings.** Psychopharmacology Bulletin. 15(3):16-19, 1979.

Abstracts from a colloquium held in Canada in November 1978 on response to antidepressant drugs (problems of predictors in therapeutic response in affective disorders: biochemical, pharmacokinetic, neurophysiological, performance, and clinical aspects) are presented. The response to antidepressant drugs was discussed in relation to plasma drug levels, urinary levels of 3-methoxy-4-hydroxyphenylglycol (MHPG), salivary electrolytes, acetylcholinesterase status, and sleep deprivation. A commentary on the significance of urinary MHPG in relation to depression is also included. 1 reference.

002090 Nuller, J. L.; Ostroumova, M. N. Bekhterev Psychoneurological Research Institute, Leningrad, USSR **Resistance to inhibiting effect of dexamethasone in patients with endogenous depression.** Acta Psychiatrica Scandinavica. 61(2):169-177, 1980.

Suppression of 11-hydroxycorticosteroids (11-OHCS) release with dexamethasone was investigated in 52 patients with endogenous depression and also in normals and in patients with other mental diseases. The suppression was considerably less in depressives than in control groups. The dexamethasone test in-

dices were normalized during remission. To elucidate mechanisms of the dexamethasone inhibiting effect, the influence of tryptophan, DOPA, and benzodiazepines on the 11-OHCS level and the degree of its suppression with dexamethasone were studied. Data indicate a dual effect of serotonin on the regulation of the adrenal function: it stimulates corticotropin releasing factor (CRF) secretion and increases the inhibiting effect of corticosteroids on CRF release. It is suggested that during depression the negative feedback is disturbed in the system of brain monoamines and glucocorticoids. The possible role of this impairment in depression pathogenesis is considered. 33 references. (Author abstract)

002091 Nurnberger, J.; Gershon, E.; Murphy, D.; Buchsbaum, M.; Goodwin, F.; Post, R.; Lake, C.; Guroff, J.; McGinniss, M. Section on Psychogenetics, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Biological and clinical predictors of lithium response in depression.** (Unpublished paper). Bethesda, MD, NIMH, 1980. 22 p.

The relative power of the following variables in the same set of patients to predict acute antidepressant response to lithium was assessed: bipolarity, family history of bipolar illness, augmenting on average evoked response (AER) testing, lithium erythrocyte/plasma ratio, platelet monoamine oxidase (MAO), erythrocyte catechol-O-methyltransferase, serum dopamine beta hydroxylase (DBH), and the MNS blood group system. In the population studied, the highest correlation with lithium antidepressant response was seen with the augmentation of the AER: no other single factor was significantly correlated with antidepressant response. Lithium erythrocyte/plasma ratio showed a nonsignificant but suggestive trend for negative correlation. The cumulative predictive power of the variables studied is impressive. The three factors of AER, MAO, and DBH account for 44% of the variance in response. These findings suggest hypotheses for replication and warrant a larger scale clinical trial. One interesting finding was that the MNS blood group system predicts about 10% of the variance in the sample. 38 references.

002092 Oppenheim, Gerald; Ebstein, Richard P.; Belmaker, Robert H. Belmaker: Jerusalem Mental Health Center-Ezrat Nashim, P.O. Box 140, Jerusalem, Israel **Effect of lithium on the physostigmine-induced behavioral syndrome and plasma cyclic GMP.** *Journal of Psychiatric Research*. 15(2):133-138, 1979.

A possible mode of action of lithium's proven prophylactic value in depression was examined by assessing the effect of pre-treatment with lithium on physostigmine-induced behavioral response. A marked physostigmine response was observed in five lithium treated, euthymic manic-depressive subjects as well as in five lithium free, normal controls, with no diminution in the lithium treated subjects. Plasma cyclic GMP, a possible product of cholinergic receptor activity, also showed no differential response in lithium treated and lithium free subjects. Results confirm recent reports that physostigmine-induced psychomotor retardation can occur in normal patients. 25 references. (Author abstract modified)

002093 Ostow, Mortimer. 5021 Iselin Ave., Riverdale, NY 10471 **Is it useful to combine drug therapy with psychotherapy?** *Psychosomatics*. 20(11):731, 735, 1979.

The effectiveness of the combination of drug therapy with psychotherapy in cases of psychosis and manic depressive illness is discussed. Successful therapy requires careful titration of dosage to accommodate both the patient's individual dose response curve and the pathogenic stress to which he is currently exposed, changes in dosage requirement depending on external stress, and a complementary relationship between drug therapy

and psychotherapy. The limited role of drug therapy in the treatment of neuroses and personality disorders is also considered. 1 reference.

002094 Overo, K. Fredricson. Biochemical Department, H. Lundbeck & Co. A/S, Ottilievej 7-9, DK-2500 Copenhagen-Valby, Denmark **Pharmacokinetic aspects on once-daily nortriptyline administration.** *Neuropsychobiology*. 6(1):34-41, 1980.

Steady state nortriptyline plasma levels were studied in 21 endogenously depressed patients treated with a single 150mg morning dose and compared to theoretical curves which were calculated from previously known kinetic data. Fairly good agreement between predicted and experimentally found concentrations was observed. The fluctuation between maximal and minimal drug levels within the dosage interval was found to be more pronounced than with a t.i.d. dosage regimen, but still limited, and the minimum levels were well compatible with published t.i.d. data. The biological half-life agreed well with previously published data for volunteers. It is concluded that once daily administration of nortriptyline results in relatively flat concentration curves as would be expected from the kinetic features of the drug. 22 references. (Author abstract modified)

002095 Pedersen, Johan Henrik; Sorensen, Jorgen Lund. Dept. of Psychiatry, Aarhus University, Psychiatric Hospital, Risskov, Denmark **Therapeutic effect and side effects in patients with endogenous depression treated with oral nortriptyline once a day.** *Neuropsychobiology*. 6(1):42-47, 1980.

The effects of once a day treatment with 150mg nortriptyline were studied using 21 patients with endogenous depression as subjects. The therapeutic effect was good and at any rate not inferior to that of dosages several times a day. Side-effects were only a little pronounced and at any rate not more marked than after dosages several times a day. It is suggested that, out of regard for the administrative and psychological advantages of the once a day dosage, this form should be preferred, particularly in outpatient treatment with nortriptyline of endogenous depression. 6 references. (Author abstract modified)

002096 Perez-de-Francisco, Cesar. Benito Perez Galdos 214, Mexico 10, D.F., Mexico **Therapy resistant depressions.** *International Pharmacopsychiatry*. 14(2):71-78, 1979.

Aspects of treating therapy resistant, or refractory, depression are examined. Classification of depression and the historical antecedents of antidepressive therapeutics are discussed. The major treatment approaches include pharmacotherapy, hormone therapy, electroconvulsive shock, sleep withdrawal, and mixed treatments. Epidemiological studies indicate that 10 to 28% of depressed patients remain refractory to these approaches. In such cases, treatment may involve increased drug dosage, reserpine in high doses, a combination of drugs with propranolol, and other recently developed modalities or tools. Genetic studies may eventually yield definitive data on the etiology of this type of depression. 26 references.

002097 Perry, Paul; Tsuang, Ming T. Tsuang: East Ward Inpatient Service, University of Iowa Psychiatric Hospital, 500 Newton Rd., Iowa City, IA 52242 **Treatment of unipolar depression following electroconvulsive therapy: relapse rate comparisons between lithium and tricyclics therapies following ECT.** *Journal of Affective Disorders*. 1(2):123-129, 1979.

A retrospective chart study and followup telephone interviews were used to compare the relapse rates of unipolar depressives who had received either lithium or tricyclics following electroconvulsive therapy (ECT). Results show no difference between the two treatment groups. Data suggest that ECT followed by either lithium or a tricyclic antidepressant is a more

effective treatment for unipolar depression than ECT alone. 17 references. (Author abstract modified)

002098 Pickar, David; Cohen, Robert M.; Murphy, Dennis L.; Fried, Deborah. Unit on Studies of Drug Abuse, Biological Psychiatry Branch, NIMH, Bldg. 10, Rm. 2N210, Bethesda, MD 20205 **Tyramine infusions in bipolar illness: behavioral effects and longitudinal changes in pressor sensitivity.** *American Journal of Psychiatry*. 136(11):1460-1463, 1979.

The behavioral effects and longitudinal changes in pressor sensitivity of tyramine infusions were examined in a patient with bipolar illness. Pressor response tests were administered during depressed and hypomanic phases of the illness. The greatest tyramine sensitivity while unmedicated occurred when the patient was hypomanic, and the least sensitivity when she was depressed before her first switch. Tyramine produced a replicable mood and cognitive alteration only in the infusion closest to the switch from hypomania to depression, suggesting that the CNS may be particularly susceptible to peripheral noradrenergic inputs at specific points in bipolar illness. It is concluded that the data raise the possibility that changes in peripheral alpha-adrenergic receptor sensitivity accompany spontaneous mood cycles. 13 references. (Author abstract modified)

002099 Potter, William Z.; Zavadil, Anthony P. III; Kopin, Irwin J.; Goodwin, Frederick K. Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **Single-dose kinetics predict steady-state concentrations of imipramine and desipramine.** *Archives of General Psychiatry*. 37(3):314-320, 1980.

Single dose prediction of ultimate steady-state concentrations of tricyclic antidepressants at the onset of treatment as a practical therapeutic as well as research tool was investigated. Such predictions were demonstrated following the tertiary amine, imipramine hydrochloride, and the secondary amine, desipramine hydrochloride, in a long-term treatment patient population. Results show that long-term treatment does not alter metabolism of either imipramine or desipramine. The relative merits of single dose predictions using total and abbreviated areas under the curve and concentration at 24 hours were also compared. 26 references. (Author abstract modified)

002100 Puhlinger, W.; Kocher, R.; Gastpar, M. Wagner-Jauregg-Krankenhaus, A-4020 Linz, Austria **Incompatibility of lithium therapy with neuroleptics.** *Zur Frage der Inkompatibilität einer Lithium-Neuroleptika-Kombinationstherapie.* *Nervenarzt*. 50(2):124-127, 1979.

The question of reliability of combination therapy with lithium and neuroleptics is discussed. The discussion is based on the case of a 64-year-old female manic-depressive patient who developed a serious organic psychosyndrome, when she was given during the manic phase, after 2 years of prophylactic treatment by lithium, additional small doses of three different neuroleptics (Haloperidol, Thiopropazine, Flupenthixol). Neither lithium alone nor the triple dose of neuroleptics alone brought about such side-effects. It is suggested that lithium and neuroleptics may be incompatible and therefore unreliable, if used in combination. The existing literature which deals with the subject has only raised the question of reliability of a special combination of lithium and Haloperidol. 11 references. (Author abstract modified)

002101 Richman, Judith; Weissman, Myrna M.; Klerman, Gerald L.; Neu, Carlos; Prusoff, Brigitte A. Division of Health Administration, Columbia University School of Public Health, New York, NY 10032 **Ethical issues in clinical trials: psychotherapy research in acute depression.** *IRB: A Review of Human Subjects Research*. 2(2):1-4, 1980.

A research study of the efficacy of psychotherapy in comparison and in combination with pharmacotherapy in treating acute depression is described. One ethical issue involved balancing two competing goals: the goal of doing good by utilizing a scientifically sound research design that would best demonstrate treatment effects, and the goal of not doing harm, or protecting the safety of research subjects. The results demonstrate that the use of a nonscheduled treatment control group in a clinical trial involving acutely depressed ambulatory patients is scientifically sound, acceptable to patients, and ethical in terms of patient safety. Model limitations are discussed. 20 references. (Author abstract modified)

002102 Roos, Bjorn-Erik; Wickstrom, G.; Hartvig, P.; Nilsson, J. L. G. Dept. of Psychiatry, University Hospital, S-750 14 Uppsala, Sweden **Quantitation of CSF concentrations and biological activity of probenecid metabolites.** *European Journal of Clinical Pharmacology*. 17(3):223-236, 1980.

The concentrations of probenecid and four of its metabolites have been examined in plasma and cerebrospinal fluid (CSF) of six patients with depressive disorders by electron capture gas chromatography after extractive methylation. The plasma concentration of each of the metabolites was in the range 1.5 to 15 mcg/ml and constituted less than 10% of the parent compound. The penetration into CSF of the metabolites was lower than that of probenecid. The concentration of each of the metabolites was below 0.2 mcg/ml and the total concentration never exceeded 10% of the probenecid concentration. The inhibitory effect of the metabolites on uptake was tested in rabbit renal cortex using 3H-p-amino-hippuric acid. The inhibitory effect was low. From the low activity and relatively low concentrations of the metabolites in CSF it is concluded that probenecid metabolites do not contribute to the probenecid-induced blocking effect of acid transport from the CSF. 12 references. (Author abstract modified)

002103 Rosenthal, Norman E.; Rosenthal, Leora N.; Stallone, Frank; Fleiss, Joseph; Dunner, David L.; Fieve, Ronald R. Clinical Psychobiology Branch, NIMH, Building 10, Room 4S239, 9000 Rockville Pike, Bethesda, MD 20205 **Psychosis as a predictor of response to lithium maintenance treatment in bipolar affective disorder.** *Journal of Affective Disorders*. 1(4):237-245, 1979.

A group of 66 bipolar I lithium clinic patients were studied for a history of psychotic symptoms at some time during the course of their illness. Agreement between different sources of information was calculated, and the patient population was divided into psychotic and nonpsychotic subgroups. Probability of remaining well on lithium for the different subgroups was analyzed by the life table method. Psychosis during mania appeared to be associated with especially good early lithium prophylaxis. 16 references. (Author abstract)

002104 Santonastaso, P.; Maistrello, I.; Battistin, L. Dept. of Neurology and Psychiatry, University of Padua Medical School, via Giustiniani, I-35100 Padua, Italy **Comparison of Valparin (valproic acid) with imipramine in the treatment of depression: a double-blind study.** *Acta Psychiatrica Scandinavica*. 60(2):137-143, 1979.

Hospitalized patients with depressive illness entered a double-blind trial to compare valproic acid hydrochloride with imipramine. Both drugs produced a statistically significant improvement in the depressive symptoms as early as the 7th day, measured by the Hamilton Rating Scale. A side-effects checklist showed no significant difference between valproic acid and imipramine. A lack of anticholinergic effects was noted in the valproic acid group although upper gastrointestinal side-effects were

more frequent. It is concluded that viloxazine is an effective antidepressant with a fairly rapid onset of action suitable for outpatient or inpatient therapy. 12 references. (Author abstract modified)

002105 Silverman, Joel J.; Brennan, Peggy; Friedel, Robert O. MCV Station, Box 710, Richmond, VA 23298 **Clinical significance of tricyclic antidepressant plasma levels.** *Psychosomatics*. 20(11):736-740, 745-746, 1979.

Literature concerned with assay methods for tricyclic antidepressants (TADs) is summarized and the current clinical usefulness of drug plasma levels in the management of depressed patients receiving TADs is evaluated. The use of TAD plasma levels is currently limited by the difficulty in obtaining quality laboratory determinations in most geographic areas. Plasma levels are most valuable in treatment of patients who have problems with lack of response to the drugs, placebo response, non-compliance, multidrug effects, and changes associated with aging. Therapeutic plasma levels of six of the most commonly used TADs (nortriptyline, imipramine, desipramine, amitriptyline, protriptyline, and doxepin) are reviewed. Side-effects and toxicity levels of TADs are considered. It is concluded that clinical application of steady state plasma level ranges should be limited to patients with endogenous depression, since data are very limited for other varieties of depressive illness. 54 references. (Author abstract modified)

002106 Singer, L.; Schlienger, J. L.; Kammerer, F.; Stephan, F. Service de Psychiatrie II, C.H.U. de Strasbourg, F-67005 Strasbourg Cedex, France **Lithium and thyroid function: benefits of the thyrotropin releasing hormone test in the diagnosis of lithium-induced thyroid dysfunctions.** *Lithium et fonction thyroïdienne: intérêts du test à la TRH dans le dépistage des dysthyroïdies lithio-induites.* *Encephale*. 5(2):171-188, 1979.

To understand the frequency and the intensity of the endocrine effects of lithium, the thyroid parameters and the steady state of the hypothalamo/pituitary/thyroid axis were tested using the TRH test in 52 patients with manic depressive psychosis with special attention to TSH, prolactin, and growth hormone. The 24 experimental subjects were treated with lithium for 1 month to 6 years while the 28 others were considered controls. The lithium treatment involves a decrease in the free thyroxine index, an increase in the mean baseline TSH level, and a noteworthy increase in the TSH responsiveness to TRH. The TSH supranormal responses were neither correlated with the length of the treatment nor with the age of the patients. They appear as the consequence of a decrease in the thyroidal hormone secretion. The basal and stimulated prolactinemia remain comparable in the two groups of patients and no response of growth hormone occurred after TRH. The TRH test must be considered as a useful complement for the surveillance of the patients treated with lithium because it permits the early diagnosis of lithium-induced thyroid dysfunction. 55 references. (Author abstract modified)

002107 Small, Joyce G.; Kellams, Jeffrey J.; Milstein, Victor; Small, Iver F. Indiana University School of Medicine, Larue D. Carter Memorial Hospital, Indianapolis, IN **Complications with electroconvulsive treatment combined with lithium.** *Biological Psychiatry*. 15(1):103-112, 1980.

A retrospective controlled study which investigated whether lithium given in combination with electroconvulsive therapy (ECT) influences side-effects and/or outcome is described, and complications with ECT and lithium are discussed. All patients receiving ECT at a university based teaching and research hospital and all patients treated with ECT by a private practitioner were reviewed. Among these 250 patients, 25 were identified

who had received lithium simultaneously with ECT. These experimental Ss were paired with others from the same population, matched for research diagnosis, age, and duration of illness. Data were culled from the medical charts concerning outcome of ECT and recorded difficulties and side-effects including pretreatment and posttreatment EEG and neuropsychological data in the hospital based sample. Comparison between experimental Ss and control Ss reveals that patients on lithium experienced more severe memory loss and atypical neurological findings than did controls. Ss also showed more impairment in neuropsychological test performance during and after ECT. Therapeutic outcome was less satisfactory in the lithium treated patients. There were no EEG differences between the groups nor were there difficulties with administration of ECT between the groups. Retrospective evidence suggests that there might be negative interaction between these two methods for the treatment and prevention of affective illness. Mechanisms whereby lithium may enhance the amnesic side-effects of ECT and possibly interfere with the therapeutic efficacy are discussed. 14 references. (Author abstract modified)

002108 Stein, Marsha K.; Rickels, Karl; Weise, Charles C. Rickels: 203 Piersol Building, Hospital of University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104 **Maintenance therapy with amitriptyline: a controlled trial.** *American Journal of Psychiatry*. 137(3):370-371, 1980.

The efficacy of amitriptyline maintenance therapy was examined in 55 nonpsychotic depressed psychiatric outpatients treated in private practice using a double-blind design. The treatment program involved a 6 week acute trial, a 2 week open therapy phase, and a 6 month maintenance phase. Data indicated that a significantly greater proportion of amitriptyline patients than placebo patients completed more than 2 months' maintenance treatment (68% versus 38%). All placebo patients who dropped out during the first 2 months had relapsed, as compared with six amitriptyline patients who had become worse and three who had continued to maintain improvement. Over the 6 month period, 28% of the amitriptyline patients as compared with 69% of the placebo patients relapsed. Neither family history, illness history, previous psychiatric treatment, presenting symptoms, nor response to acute treatment were significantly related to maintenance treatment outcome. 10 references.

002109 Strzyzewski, Włodzimierz; Rybakowski, Janusz; Kapelski, Zdzisław. Dept. of Psychiatry, Academy of Medicine, ul. Szpitalna 27/33, 60-572 Poznań, Poland **Investigations on electrolyte and water contents in plasma and red blood cells in the course of thymoleptic treatment of depressive syndromes.** *Neuropsychobiology*. 6(3):121-127, 1980.

Water and electrolyte contents in plasma and red blood cells (RBC) were studied in 46 patients with depressive syndromes of various etiology (bipolar, unipolar, psychogenic) before and after 14 days of imipramine treatment. Initial low RBC sodium levels were characteristic of patients with bipolar depression. A significant increase in RBC sodium was observed after imipramine treatment in a group of good imipramine responders. RBC sodium changes in psychogenic patients after imipramine were different from those observed in endogenous (bipolar plus unipolar) ones. A fall in plasma calcium levels was shown in the course of imipramine administration mostly in patients with favorable response to the drug. 22 references. (Author abstract)

002110 Targum, Steven D.; Davenport, Yolande B.; Webster, Marian J. Psychiatric Institute, 4460 MacArthur Boulevard, N.W., Washington, DC 20007 **Postpartum mania in bipolar manic-depressive patients withdrawn from lithium carbonate.** *Journal of Nervous and Mental Disease*. 167(9):572-574, 1979.

The perinatal course of three women with previously diagnosed bipolar I manic-depressive illness who were withdrawn from lithium carbonate maintenance therapy immediately prior to pregnancy is described. The patients had been euthymic while on lithium carbonate for at least 3.5 years prior to their pregnancies. Two of the three patients developed a manic syndrome within 2 weeks postpartum. The use of lithium carbonate during pregnancy, and particularly in the postpartum period, requires reassessment. An ongoing clinical relationship and the reinstitution of lithium in the third trimester in most cases is advocated. 9 references. (Author abstract modified)

002111 Taylor, John W. 19 Grantham Street, Burwood, N.S.W. 2134, Australia **Mental symptoms and electrolyte imbalance.** Australian and New Zealand Journal of Psychiatry. 13(2):159-160, 1979.

A case history of a 75-year-old woman on long-term diuretic therapy who presented with depression is presented. She was found to have hyponatraemia and hypochloreaemia. No improvement in her condition was gained with antidepressant medication, but it is reported that she responded promptly to cessation of spironolactone and prescription of potassium chloride. It is concluded that elderly patients with mental symptoms should not be presumed to have untreatable chronic disease, but should be assessed to discover any treatable problem that may be contributing to their symptoms. Long-term diuretic therapy without monitoring of serum electrolytes is noted to be particularly dangerous. 5 references. (Author abstract modified)

002112 Trapp, George A.; Handorf, Charles R.; Larach, Veronica. Veterans Administration Hospital, Shreveport, LA **Trazodone in the treatment of depressed inpatients.** Psychopharmacology Bulletin. 15(3):25-27, 1979.

The effects of trazodone, imipramine, and placebo were compared in a randomized double-blind trial in 30 depressed male inpatients, aged 22 to 65 years. Scores on the Hamilton Depression Scale revealed a therapeutic response in 6 of 10 patients treated with trazodone, 6 of 10 treated with imipramine, and 4 of 10 given placebo. All patients taking imipramine showed anticholinergic side-effects, but the frequency of treatment emergent symptoms in trazodone treated patients was similar to that seen with placebo. The antidepressant efficacy of trazodone was not established in this study, due to the high placebo response rate, but the excellent patient tolerance of the drug supports further study. 1 reference.

002113 Turkington, Roger W. Diabetes Center, St. Francis Hospital, 3237 South 16th Street, Milwaukee, WI 53215 **Depression masquerading as diabetic neuropathy.** Journal of the American Medical Association. 243(11):1147-1150, 1980.

Fifty-nine patients referred for painful diabetic neuropathy of the lower extremities were evaluated for depression and response to antidepressant drug therapy in a double-blind controlled study. All patients were found to have substantial degrees of depression during psychiatric interview and by Kupfer-Detre test scores. Treatment with imipramine hydrochloride or amitriptyline hydrochloride resulted in complete remission of lower extremity pains in all patients in 8 to 12 weeks, with concomitant relief of depression and return of depression test scores to that of the controls. These results suggest that the syndrome of painful diabetic neuropathy of the lower extremities represents a depressive equivalent in a large proportion of cases and that treatment with imipramine or amitriptyline is a successful mode of therapy for such persons. 13 references. (Author abstract modified)

002114 Tyrer, Stephen P.; McCarthy, Martin J.; Shopsin, Baron; Schacht, Robert G. Dept. of Psychiatry, New York Uni-

versity Medical Center, New York, NY 10016 **Lithium and the kidney.** Lancet. No. 8159:94-95, 1980.

Results of a study of the effects of lithium on kidney function are reported. Kidney function was compared for 48 manic-depressive patients receiving lithium for 5 years or more and a control group of affectively ill patients (predominantly unipolar and taking tricyclics). An analysis of covariance, with age as the covariate, showed that lithium had a significant effect on renal concentration capacity, regardless of patient sex. It is, however, suggested that the clinical relevance of this finding may be overestimated: an abnormal result does not warrant alarm or change of treatment if this is the sole finding. 1 reference.

002115 van Kammen, Daniel P.; Murphy, Dennis L. NIMH, Biological Psychiatry Br., 9000 Rockville Pike, Building 10, Bethesda, MD 20205 **Prediction of antidepressant response to lithium carbonate by a 1-day administration of d-amphetamine in unipolar depressed women.** Neuropsychobiology. 5(5):266-273, 1979.

Evidence of a moderate relationship between the self-rated activation and euphoria responses to the acute administration of d-amphetamine and the antidepressant responses to a lithium carbonate is presented. A 3 week clinical trial was conducted with female unipolar depressed patients. Responses to d-amphetamine and lithium were not correlated in male patients or in bipolar patients. This preliminary finding must be replicated before further conclusions can be drawn. 41 references. (Author abstract modified)

002116 VonKnorring, L. Dept. of Psychiatry, University of Umea, S-90185, Umea, Sweden **A double-blind trial: Valavan against placebo in depressed elderly patients.** Journal of International Medical Research. 8(1):18-21, 1980.

A double-blind controlled study of viloxazine against placebo was conducted with elderly patients with a primary diagnosis of depression. Significant improvements in depression ratings were noted in the viloxazine group after 3 weeks. Viloxazine was effective and well tolerated at doses of 100 to 200mg in these Ss, several of whom had concurrent cardiac disease. 17 references. (Author abstract modified)

002117 Wallin, L.; Alling, C. Psychiatric Research Centre, St. Jorgen's Hospital, S-442 03 Hisingen Backa, Sweden **Effect of sustained-release lithium tablets on renal function.** British Medical Journal. No. 6201:1332, 1979.

Readily soluble lithium carbonate tablets were compared with sustained release tablets to determine whether more stable plasma concentrations and less pronounced lithium concentration peaks might reduce toxic effects. Twenty-eight pairs of patients being treated with long-term lithium and in whom plasma lithium concentrations had always been within the therapeutic range were paired for age, sex, and total lithium intake. It was found that sustained release lithium tablets produced less impairment of the ability of the kidney to concentrate urine than did lithium carbonate tablets. The sustained release tablets also gave more stable plasma concentrations and fewer concentration peaks than lithium carbonate tablets. 5 references.

002118 Weissman, Myrna M. Dept. of Psychiatry, Yale University School of Medicine, 904 Howard Avenue, New Haven, CT 06519 **The psychological treatment of depression: evidence for the efficacy of psychotherapy alone, in comparison with, and in combination with pharmacotherapy.** Archives of General Psychiatry. 36(11):1261-1269, 1979.

Seventeen clinical trials are identified that test the efficacy of various psychological treatments (behavioral, cognitive, group, marital, interpersonal) alone, in comparison with, and in combination with pharmacotherapy in homogeneous samples of de-

pressed outpatients. In all of the studies reported, psychotherapy was more efficacious than no active treatment. Results suggest that combination treatment (tricyclic antidepressants and psychotherapy) is the most efficacious treatment. 36 references. (Author abstract modified)

002119 Weizman, A.; Weizman, R.; Tyano, S.; Wijsenbeek, H. Tyano: Adolescent Dept., Gehah Psychiatric Hospital, Petah-Tikva, Israel **Bipolar depression (manic-depressive disease) in early adolescence**. *Adolescence*. 14(55):617-620, 1979.

Three rare cases of bipolar depression in early adolescence are reported. All developed at age 13 to 14 years, and the incidence of the cases over a 3-year period at one hospital's adolescent unit should alert professionals to the possibility of such a disorder in teenage patients. Diagnosis is crucial in order to administer the required treatment in the acute phase and the preventive treatment afterwards. Therapeutic approaches are similar to those used with adults, and drug dosages are the same. 10 references.

002120 Wirz-Justice, Anna; Arendt, Josephine. University Psychiatric Clinic, Basle, Switzerland **Plasma melatonin and antidepressant drugs**. *Lancet*. No. 8165:425, 1980.

Plasma melatonin data obtained after acute and chronic antidepressant treatment are presented in a letter to the editor. A bimodal seasonal variation, with low values in spring and autumn, in melatonin secretion has been found and this suggests that time of year must be controlled if spurious conclusions are to be avoided. A preliminary study of untreated depressive patients, corrected for month of year, still showed significantly lower early morning melatonin values in depressives compared to controls. Bipolar patients showed a considerable scatter in the depressive stage and high to normal values in the hypomanic stage. In a followup of three patients treated with maprotiline, results indicated that all three were nonresponders, remained depressed, and showed undetectable melatonin both before and during treatment. In studies in the rat, maprotiline increased pineal and plasma melatonin following acute administration; while chronic treatment with clomipramine reduced rat pineal melatonin. It is suggested that if circadian rhythm of melatonin is a marker for the function of the central circadian pacemaker, it should be considered in relation to other timing changes in depression. The question of timing rather than amount is important in view of evidence that antidepressant drugs slow down the circadian pacemaker. 5 references.

002121 Wirz-Justice, Anna; Puhringer, Wolfgang; Hole, Gunter. Clinical Psychobiology Branch, NIMH, Bethesda, MD **20205 Response to sleep deprivation as a predictor of therapeutic results with antidepressant drugs**. *American Journal of Psychiatry*. 136(9):1222-1223, 1979.

A positive response to sleep deprivation in 34 depressive patients was examined as a predictor of therapeutic results with antidepressant drugs. Of the sleep deprivation responders, 24 improved after subsequent tricyclic antidepressant treatment. In contrast, 12 of 18 nonresponders to sleep deprivation also failed to improve with long-term drug treatment. The improvement after 1 night's sleep deprivation and after chronic tricyclic drug treatment may be the result of a similar mechanism of action through phase advance of the circadian sleep/wake cycle. It is concluded that this preliminary experimental evidence lends support to the clinically observed relationship. 10 references.

002122 Woggon, B.; Angst, J. Psychiatrische Universitätsklinik, Forschungs Abt., Zurich, Switzerland **Comparative efficacy of nomifensine and imipramine**. *Psychopharmacology Bulletin*. 15(3):29-31, 1979.

Thirty newly-hospitalized depressed patients were treated for 30 days with nomifensine or imipramine, with a mean daily dose of 150mg of either drug. Patients were tested on the Hamilton Rating Scale for Depression and the AMP-System on days 0, 10, 20, and 30. Patients treated with nomifensine showed greater improvement in concentration, memory, cognition, anxiety, and restlessness after 10 days of treatment, but those given imipramine showed more improvement in symptoms associated with depressed mood. The effects of the two drugs were similar after 20 days, but improvement was more marked with imipramine after 30 days. Nomifensine caused fewer side-effects than imipramine. 10 references.

002123 Wold, Patricia Neely; Dwight, Kirby. Community Mental Health Clinic, 2741 Pawtucket Ave., East Providence, RI 02914 **Subtypes of depression identified by the KDS-3A: a pilot study**. *American Journal of Psychiatry*. 136(11):1415-1419, 1979.

The use of the Kupfer Detre Scale (KDS-3A) to identify subtypes of depression was examined. The scale was administered to depressed outpatients at intake and after 1, 3, and 6 months of treatment with either tricyclic antidepressants or lithium carbonate. None of the 10 tricyclic responders scored below 8 on the 14 point chronic anxiety scale at intake while seven of the 12 lithium responders did, suggesting that any patient scoring below 8 is a probable candidate for lithium therapy. Patients scoring 8 or above on the chronic anxiety scale fell into two categories: those who had a low impulsivity score and responded to tricyclic antidepressants and those who had a high impulsivity score, responded to lithium, and had cyclothymic disorder or emotionally unstable character disorder. It is concluded that the KDS-3A can be used at intake as a guide to the choice of medication for depressed patients. 11 references. (Author abstract modified)

002124 Worrall, Ernest P.; Moody, J. P.; Peet, M.; Dick, Peter; Smith, Anne; Chambers, Catherine A.; Adams, Malcolm; Naylor, Graham J. University of Glasgow Dept. of Psychological Medicine, Southern General Hospital, Glasgow G51 4TF, Scotland **Controlled studies of the acute antidepressant effects of lithium**. *British Journal of Psychiatry*. 135(September):255-262, 1979.

The major acute antidepressant effects of lithium were demonstrated in two randomized double-blind controlled trials on 63 depressed female inpatients subject to recurrent affective disorder (bipolar and unipolar manic depressive psychosis). At the end of 3 weeks, lithium produced more uniform improvement than imipramine. Lithium in combination with tryptophan (in the form of Optimax) was superior to tryptophan alone, with the latter drug having no discernible antidepressant activity in this group of patients. Lithium did not produce an antidepressant effect until the second and third week of both trials. 34 references. (Author abstract modified)

002125 Young, J. P. R.; Lader, M. H.; Hughes, W. C. Dept. of Psychological Medicine, St. Thomas's Hospital, London SE1, England **Controlled trial of trimipramine, monoamine oxidase inhibitors, and combined treatment in depressed outpatients**. *British Medical Journal*. No. 6201:1315-1317, 1979.

One-hundred-thirty-five mildly or moderately depressed outpatients were randomly allocated to one of five groups receiving 6 weeks' treatment with antidepressant drugs. The groups received a tricyclic antidepressant (trimipramine, mean dose 106mg at night) or a monoamine oxidase inhibitor (MAOI) (phenelzine or isocarboxazid, mean doses 45 and 32mg/day, respectively), or a combination of the two (phenelzine plus trimipramine or isocarboxazid plus trimipramine). Various scales

were used to measure depression before and at 1, 3, and 6 weeks of treatment, and results were assessed blindly. The tricyclic antidepressant was found to be consistently superior to the MAOIs and the combined treatments. Some differential indicators of response to the various antidepressants are reported. It is concluded that neither MAOIs nor MAOIs combined with tricyclic antidepressants are the treatment of first choice in unselected outpatients with mild or moderate depression. 17 references. (Author abstract modified)

002126 Zis, Athanasios P.; Cowdry, Rex W.; Wehr, Thomas A.; Muscettola, Giovanni; Goodwin, Frederick K. Clinical Psychobiology Branch, NIMH Building 10, Room 4S239, 9000 Rockville Pike, Bethesda, MD 20205 **Tricyclic-induced mania and MHPG excretion.** *Psychiatry Research*. 1(1):93-99, 1979.

In order to evaluate the presumed involvement of altered noradrenergic receptor sensitivity in the switch process from depression into mania, the relationship between pretreatment 3-methoxy-4-hydroxy-phenylglycol (MHPG) and tricyclic-induced mania or hypomania in bipolar depressed patients was explored. Within the groups of patients developing mania or hypomania on tricyclics, there was a strong positive correlation between pretreatment 24 hour urinary MHPG and the latency of onset of the episode. This finding is consistent with both the reported differences in MHPG excretion between unipolar and bipolar patients and the postulated noradrenergic involvement in the switch process. 26 references. (Author abstract modified)

10 DRUG TRIALS IN NEUROSES

002127 Butter, Hendrik J. Centre Hospitalier Pierre Janet, Hull, Quebec, Canada **A multiple discriminant analysis of psychometric and psychophysiological functioning of psychiatric patients.** *Psychiatric Journal of the University of Ottawa*. 4(3):239-247, 1979.

Stress performance was examined as a function of psychophysiological performance among normal controls and four groups of psychiatric patients: nonmedicated, minor tranquilizer, antipsychotic, and antidepressant medication. Two IQ subtests were used as tasks of stress. Results showed introverted psychiatric patients manifested a higher degree of emotional lability and somatic reactivity than did introverted normal controls, and that both psychometric and psychophysiological dependent variables predictively discriminated patients who were on antidepressant medication from patients receiving antipsychotic and minor tranquilizing psychoactive agents. These findings are in accord with the usage of an inductive/deductive/functional rationale to improve psychiatric diagnosis and treatment. 8 references. (Author abstract)

002128 Costa, Erminio. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **The present status of neurohumoral transmission.** (Unpublished paper). Washington, DC, NIMH, 1980. 23 p.

The status of neurohumoral transmission is reviewed with emphasis on modulation of receptor function. Topics discussed include: neurotransmitters and receptors; polypeptides as putative neurotransmitters; and coexistence of two transmitters in one axon and the function of related receptors. Also covered are: molecular heterogeneity of peptide neurotransmitter stores; the role of specific membrane constituents in neuronal communication; and regulation of dopamine receptors by calmodulin. Data are also given on: internalization of beta-adrenergic receptors as a mechanism of receptor subsensitivity; and regulation of GABA receptors. 41 references.

002129 d'Elia, G.; Lehmann, J.; Raotma, H. Dept. of Psychiatry, N-5016 Haukeland Hospital, Bergen, Norway **Bimodal dis-**

tribution of serum tryptophan level. *Acta Psychiatrica Scandinavica*. 60(1):10-16, 1979.

Serum levels of total L-tryptophan (L-TP) were determined before and during treatment in patients suffering from endogenous depression, who were treated with L-TP, 6g daily, and unilateral electroconvulsive therapy (ECT). The gaussian curve of initial L-TP concentrations changed into a bimodal distribution during treatment. The patients with initially lower L-TP levels also had lower L-TP levels during the treatment, thus forming the low concentration group within the bimodal distribution. In the patients with higher initial concentrations, the L-TP levels increased to a much greater degree, forming the high concentration group. Patients in this group needed a larger number of ECT's, probably owing to L-TP's property of shortening the seizure duration. No other background data or clinical variables showed significant differences between the groups. It is suggested that the bimodality of L-TP levels is genetically determined. 11 references. (Author abstract)

002130 Goldberg, Harold L.; Finnerty, Richard J. West-Ros Park Mental Health Center, 26 Central Avenue, Hyde Park, MA 02136 **The comparative efficacy of buspirone and diazepam in the treatment of anxiety.** *American Journal of Psychiatry*. 136(9):1184-1187, 1979.

Buspirone, diazepam, and a placebo were randomly assigned to 18, 20, and 18 adult psychoneurotic outpatients with a primary diagnosis of anxiety neurosis to test their comparative efficacy. A battery of tests administered weekly indicated that buspirone, a new agent not chemically related to any currently marketed drugs, was as effective an antianxiety agent as diazepam and produced no more and perhaps fewer side-effects. Buspirone showed excellent antidepressant effects as well. If further studies confirm these findings and determine that buspirone does not result in tolerance and addiction, it would be more advantageous than the benzodiazepines in the treatment of anxiety. 6 references. (Author abstract modified)

002131 Janosko, Rudolph E. M. Dept. of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA **Therapy for paranoia.** *Psychiatric Annals*. 9(12):28-31, 35, 1979.

The diagnosis and treatment of paranoia are discussed. Treatment must follow the establishment of a diagnosis and the careful assessment of risk, and factors indicating risk are reviewed. Establishment of a therapeutic alliance may be more difficult when either physical or chemical restraints are used. Intervention, whether individual, group, or family, begins with an opening phase during which a trusting rapport is established, then proceeds to the widening of the focus of conflict beyond the delusion, through the identification processes, and continues on to a final stage of emotional growth or, at least, social competence. Psychopharmacologic treatment is also discussed. 13 references.

002132 Mukherjee, P. K.; Holland, R. P. C. Monklands District General Hospital, Airdrie and Hartwood Hospital, Shotts, England **Study of depression.** *Journal of International Medical Research*. 7(6):588-591, 1979.

Twenty elderly depressed patients were treated with 150 to 200mg doses of Vivalan (viloxazine) on a daily basis. Significant decreases in Hamilton and Zung ratings occurred by the seventh day of treatment and further improvements were noted over the next 2 weeks. These changes were also reflected in global assessments. Headache was reported in six patients and nausea in three. Vivalan had no significant effect upon blood pressure and absence of anticholinergic side-effects proved an advantage in the treatment of these patients. 14 references. (Author abstract modified)

002133 Porot, M.; Perol, Y. no address /Prolonged clinical use of bromazepam./ Utilisation clinique prolongee du bromazepam (Ro 05 3350). *Annales Medico-Psychologiques*. 137(5):516-518, 1979.

The effects of the use of bromazepam were examined statistically in 88 cases since the end of 1967. In 79 cases, the patients took bromazepam for more than 2 years. The daily dose varied from 3 to 36mg. Findings show bromazepam gave 82% good results in cases of anxieties with physical manifestations, 67% good results in excitomotoric manifestations, and 90% good results in sleep disorders. There was never any complication. Some secondary effects at the beginning disappeared when the dose remained perfectly effective without any increase. It is concluded that bromazepam is a benzodiazepine which is remarkably effective in all manifestations of anxiety. It is one of the best hypnotics available at present.

002134 Schjonsby, H. P.; Gordon, A. E.; Koeppen, D. Distriktslegen i Ringsaker, N-2380 Brumudal, Norway A three-month double-blind study of clobazam versus diazepam in out-patients suffering from neurotic disturbances. *Journal of International Medical Research*. 7(5):404-410, 1979.

Efficacy and safety of the 1.5 benzodiazepine, clobazam, in comparison to the 1.4 benzodiazepine, diazepam, were controlled in 60 psychiatric outpatients over a period of 3 months. In the course of this long treatment period data were obtained confirming findings of shorter studies. Global assessment of the therapeutic efficacy and the total scores of the Hamilton Anxiety Scale revealed no significant difference between the compounds. Both groups showed a significant (p less than .01) improvement in the total scores of the Hamilton Anxiety Scale after 2 weeks of treatment. Scores of the individual items indicated distinct spectra of action: clobazam was more effective in diminishing anxious mood, whereas diazepam was better able to influence muscular symptoms of anxiety. The relevance of the findings for a more individualized therapy is noted. 14 references. (Author abstract modified)

002135 Shevitz, Stewart A.; Jameison, Robert C.; Petrie, William M.; Crook, James E. Psychiatry Associates of Eugene, 1059 Hilyard, Eugene, OR 97401 Compulsive water drinking treated with high dose propranolol. *Journal of Nervous and Mental Disease*. 168(4):246-248, 1980.

A patient with recurrent life threatening water intoxication secondary to compulsive water drinking (psychogenic polydipsia) is described. This patient responded well to nearly 1g of propranolol daily with a decrease in her drinking behavior, reduced sensation of thirst, and a reduction in delusional thinking. The rationale for the choice of treatment in this patient is reviewed. 17 references. (Author abstract modified)

002136 Stern, R. S.; Marks, I. M.; Mawson, D.; Luscombe, D. K. St. George's Hospital, London, England Clomipramine and exposure for compulsive rituals: II. Plasma levels, side effects and outcome. *British Journal of Psychiatry*. 136(February):161-166, 1980.

Plasma levels were obtained for 40 obsessive compulsive ritualizers, who received nightly placebo or clomipramine up to 225mg nocte for 8 months and who received behavioral treatment (exposure in vivo) from weeks 4 to 10. Plasma concentrations of clomipramine and its primary metabolite N-desmethylelomipramine steadily increased over the first 4 weeks of treatment after which they remained relatively steady. Plasma levels correlated significantly with dose and with outcome but not with side-effects. Patients with plasma clomipramine levels in the range 100 to 250ng/ml and N-desmethylelomipramine levels between 230 to 550ng/ml were

found to improve significantly more than patients outside these ranges, thus suggesting a therapeutic window for clomipramine and its primary metabolite. 9 references. (Author abstract modified)

002137 Tallman, John F.; Paul, Steven M.; Skolnick, Phil; Gallagher, Dorothy W. Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20205 Receptors for the age of anxiety: pharmacology of the benzodiazepines. *Science*. 207(4428):274-281, 1980.

Studies concerned with the effects, neurochemistry, pharmacology, and use of benzodiazepines are reviewed. Investigation of the actions of the benzodiazepines has provided insights into the neurochemical mechanisms underlying anxiety, seizures, muscle relaxation and sedation. Behavioral, electrophysiological, pharmacological, and biochemical evidence indicates that the benzodiazepines exert their therapeutic effects by interacting with a high affinity binding site of the brain. The benzodiazepine receptor interacts with a receptor for gamma-aminobutyric acid, a major inhibitory neurotransmitter and enhances its inhibitory effects. The benzodiazepine receptor may also interact with endogenous substances and several naturally occurring compounds, including the purines and nicotinamide. Both the purines and nicotinamide possess some benzodiazepinelike properties in vivo, although further work will be required to confirm their possible roles as endogenous benzodiazepines. 109 references. (Author abstract modified)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

002138 Aman, Michael G. Dept. of Psychiatry, School of Medicine, University of Auckland, P.B., Auckland, New Zealand Psychotropic drugs and learning problems -- a selective review. *Journal of Learning Disabilities*. 13(2):87-97, 1980.

The research relating to psychotropic drug effects on academic attainment in children with pronounced learning problems is reviewed. The review includes laboratory studies on stimulants, antidepressants, and antipsychotics; followup studies with hyperactive populations; and problems of diagnosis in the field of special education and difficulties which accompany labeling. The overall results of such research suggest little proof that medication is useful in treating learning problems in children. Psychoactive drugs may be beneficial to academic attainment in cases in which behavioral deviancy interferes with cognitive function, but even this remains to be demonstrated. When medication is provided to treat learning problems, it should be administered in conjunction with an acceptable form of educational therapy. 64 references.

002139 Aman, Michael G.; Singh, Nirbhay N. Department of Psychiatry, School of Medicine, University of Auckland, P.B., Auckland, New Zealand The usefulness of thioridazine for treating childhood disorders -- fact or folklore? *American Journal of Mental Deficiency*. 84(4):331-338, 1980.

Studies of thioridazine (Mellaril) use for treating childhood behavior disorders are reviewed with special emphasis on methodology. The caliber of these studies has generally been unsatisfactory, and measures of drug effect have tended to emphasize global rather than specific changes, resulting in little qualitative information being available. Examination of subgroups of children treated with thioridazine failed to reveal different levels of drug responsiveness. Few investigators have attempted to assess cognitive effects, but the evidence suggests that cognitive dulling may be an undesirable effect of treatment. It is concluded that further research of sufficient quality is needed. 32 references. (Author abstract modified)

002140 Amsterdam, Jay; Mendels, Joe. Affective Diseases Research Unit, Veterans Administration Hospital, University and Woodland Aves., Philadelphia, PA 19104 **Treatment-resistant tardive dyskinesia: a new therapeutic approach.** *American Journal of Psychiatry*. 136(9):1197-1198, 1979.

A case of tardive dyskinesia is reported which illustrates both the hazards of inappropriate use of neuroleptics and a new and successful treatment for long-term drug resistant tardive dyskinesia. After 7 years of treatment for depression with a variety of neuroleptics, sometimes in combination with other drugs, a 58-year-old woman developed constant blepharospasm and dyskinetic movements of the lower face, mouth, and tongue. Baclofen, a derivative of gamma-aminobutyric acid, was administered in slowly increasing doses to 20 mg t.i.d., resulting in a startling reversal of symptoms. Pharmacologic mechanisms are discussed. 9 references.

002141 Andrasik, Frank; Ollendick, Thomas H.; Turner, Samuel M.; Hughes, John R. Dept. of Psychology, State University of New York, Albany, NY 12222 **Pharmacological treatment of aggressive behavior and emesis in the Cornelia de Lange syndrome.** *Journal of Nervous and Mental Disease*. 167(12):764-766, 1979.

The pharmacological treatment (chlorpromazine and fluphenazine decanoate) of aggressive behavior and emesis in the Cornelia de Lange syndrome is illustrated by a case report. Institution of the neuroleptics, following an unsuccessful trial of diazepam, produced reductions of 95% and 38% for aggressive behavior and emesis, respectively. Four followup observations, occurring at 3 week intervals, revealed maintenance of low rates of aggressive behavior and continued reductions in emesis (mean reduction of 81%). These findings are notable for their inclusion of direct behavioral observation as the data base, and for the initial promising effects of neuroleptics for a rare mental retardation. 6 references. (Author abstract modified)

002142 Beal, Donald Gordon. Texas Tech University **The effect of methylphenidate hydrochloride on objective task learning, interpersonal learning and judgment behavior of hyperkinetic children.** (Ph.D. dissertation). Dissertation Abstracts International. 40(2):902-B, 1979. Ann Arbor, Univ. Microfilms No. 7917310, 284p., 1978.

The effects of methylphenidate hydrochloride (Ritalin) on the judgment behavior of hyperkinetic children were investigated in 44 male children who had received a diagnosis of hyperkinetic reaction of childhood. In a double-blind procedure, Ss were administered Ritalin or placebo for 4 weeks and assessed in a multiple cue probability learning task, an interpersonal conflict task, and an interpersonal learning task. In the multiple cue probability learning task, the medication was associated with a decrease in judgment behavior relative to the placebo group. In the interpersonal conflict and interpersonal learning tasks, the performance appeared to be a function of age of child and drug dosage. (Journal abstract modified)

002143 Beasley, B. L.; Nutt, J. G.; Davenport, R. W.; Chase, T. N. Chase: Dept. of Neurology, NIH, Bethesda, MD 20205 **Treatment with tryptophan of levodopa-associated psychiatric disturbances.** *Archives of Neurology* 37(3):155-156, 1980.

The effect of 2 to 6g of tryptophan per day on levodopa-induced psychiatric symptoms was tested in nine patients with Parkinson's disease in a double-blind placebo controlled trial. The psychiatric disturbances were rated on the Brief Psychiatric Rating Scale and posttreatment assessment indicated no great alteration in symptoms as a result of tryptophan administration. 12 references. (Author abstract modified)

002144 Beitman, Bernard D.; Carlin, Albert S. Department of Psychiatry and Behavioral Sciences, RP-10, University of Washington, Seattle, WA 98195 **Night terrors treated with imipramine.** *American Journal of Psychiatry*. 136(8):1087-1088, 1979.

A case study of a 62-year-old woman who was treated successfully with imipramine for night terrors is reported. The more frequently used stage four reducing drug diazepam was not effective. But imipramine at low doses eliminated her sleeping problem. 3 references.

002145 Benkert, O.; Witt, W.; Adam, W.; Leitz, A. Psychiatric Clinic, University of Munich, Nussbaumstrasse 7, D-8000 Munich 2, Germany **Effects of testosterone undecanoate on sexual potency and the hypothalamic-pituitary-gonadal axis of impotent males.** *Archives of Sexual Behavior*. 8(6):471-479, 1979.

A double-blind comparison of the effects of testosterone undecanoate (TU) and placebo on sexual potency of 29 impotent men between the ages of 45 and 75 years is described. All patients (selected on the basis of a reduced or nonexistent capacity to have an erection during intercourse and no clinical signs of endocrinological pathology) received placebo for 2 weeks. TU was given at a daily dose of 120mg to 13 patients while the other patients continued to receive placebo. After 8 weeks, all patients received placebo again for 2 weeks. An improvement in sexual potency was reported by five patients given TU and eight patients given placebo, with no significant differences between the groups. Treatment with TU influenced neither the hypothalamic/pituitary/gonadal axis, as judged by levels of prolactin, LH, FSH, and the LHRH induced LH/FSH response, nor depression, anxiety, and somatic scores or performance tests. The only specific effect of TU treatment was to decrease the total testosterone level. 24 references. (Author abstract modified)

002146 Bianchi, G. N. 142 Ferny Avenue, Surfers Paradise, Queensland 4217, Australia **Drugs for mental disorders of old age.** *Current Therapeutics*. 20(4):73-75, 1979.

Symptoms and treatment of mental disorders common in the elderly (delirium, dementia, depression, and insomnia) are summarized. Delirium may be caused by a variety of factors ranging from drug effects through illness and sensory deprivation. Treatment is that of the underlying cause, but symptomatic control can be achieved by chlormethiazole or thioridazine. Except for those treatable cases, management of dementia is by psychotherapy; haloperidol may be used for management of paranoid symptoms, trifluoperazine or phenothiazine for emotional lability. Because of its sedative properties and lower cardiotoxicity, doxepin may be preferable to other tricyclics in the treatment of depression. Isocarboxazid should be considered in cases not responsive to tricyclics. While lithium may prove valuable for those prone to recurrent affective disorders, caution is advised in its use. Poor sleep is a normal feature of aging and hypnotics should only be given for a limited time. Nighttime sedation may be achieved with thioridazine, flurazepam, nitrazepam, or dichloralphenazone.

002147 Brambilla, F.; Zanoboni, A.; Zanoboni-Muciaccia, W.; De Maio, D. Ospedale Psichiatrico Provinciale Affori, Italy **Growth hormone response to thyrotropin-releasing hormone and gonadotropin-releasing hormone stimulation in heroin addicts.** *Neuropsychobiology*. 6(3):152-158, 1980.

The growth hormone (GH) response to thyrotropin releasing hormone (TRH) and gonadotropin releasing hormone (GnRH) was investigated in 23 male heroin addicts. Ss were between the ages of 18 and 40 years, with histories of addiction to heroin alone for 8 months to 4 years, and daily i.v. heroin intakes between 200 and 2,500mg of the drug (containing 18% pure

heroin). Eight patients received TRH 500 mcg, GnRH 150 mcg and five patients saline only, intravenously; and GH levels were assayed radioimmunologically in blood samples taken 30 minutes before, at the moment of stimulation, and 15, 30, 60, 90, and 120 minutes after administration. Results show normal basal GH levels. Stimulation with TRH and GnRH induced marked GH hypersecretion in eight of 18 patients examined. These results suggest that the hypothalamopituitary function may be impaired in heroin addiction. 38 references. (Author abstract modified)

002148 Braz-de-Lima, Jose Mauro; Oliveira, Clovis; Alves-Duro, Luiz Antonio; de Mesquita Piores, Natalia. Inst. de Neurologia Deolindo Couto, Av. Venceslau Bras 95, Botafogo, 22290 Rio de Janeiro, RJ, Brazil / **Therapeutic effect of barboxalclon in the treatment of refractory epilepsy.** / Efeito do barboxalclon nas crises convulsivas de difícil controle. Arquivos de Neuro-Psiquiatria. 38(1):89-92, 1980.

A therapeutic trial of barboxalclon with patients experiencing grand-mal seizures who had failed to respond well to other drugs, is described. Barboxalclon was administered in combination with either acetazolamide, phenobarbital, or nitrazepam. Very good results were obtained in 64% (seven) of the patients. Side-effects were minimal. 7 references. (Journal abstract modified)

002149 Brown, C. C.; Horrom, N. J.; Wagman, A. M. I. no address **Effects of L-tryptophan on sleep onset insomniacs.** Waking and Sleeping. 3(2):101-108, 1979.

The effectiveness of L-tryptophan as a hypnotic drug was tested in 18 female subjects with demonstrated laboratory sleep onset latency greater than 20 minutes. Standard sleep recordings were made on 10 nights over a 3 month period with lights out occurring 20 minutes after drug administration. Neither dosage of L-tryptophan differed from placebo as to the amount of rapid eye movement (REM), slow wave sleep or wakefulness, but the largest dose significantly reduced sleep onset latency on some of the nights. Those subjects with latencies longer than 40 minutes had the greatest reduction in latency and also evidenced high levels of anxiety on the Taylor Manifest Anxiety Scale initially. Subjects with latency between 20 and 40 minutes appeared to receive the longest lasting hypnotic effect from the higher dose. 17 references. (Author abstract modified)

002150 Brown, Ronald T.; Sleator, Esther K. Institute for Child Behavior and Development, University of Illinois at Urbana-Champaign, 51 Gerty Dr., Champaign, IL 61820 **Methylphenidate in hyperkinetic children: differences in dose effects on impulsive behavior.** Pediatrics. 64(4):408-411, 1979.

The hypothesis that a low dose of methylphenidate (.3mg/kg) is superior to a high dose (1.0mg/kg) or placebo in decreasing error scores of hyperactive children on the matching familiar figures test (MFF), a primary index of impulsivity, was tested with 11 hyperactive children. The hypothesis was verified in that the low dose reduced the number of errors on the MFF significantly more than did placebo or the high dose. It is concluded that for both learning and impulsivity in hyperactive children, the lower doses of the two doses produces the preferable effect. 35 references. (Author abstract)

002151 Brown, Ronald Terry. Georgia State University **A comparison of differential treatment approaches for impulsive responding of hyperactive children at two age levels.** (Ph.D. dissertation). Dissertation Abstracts International. 39(7):4176-A, 1979. Ann Arbor, Univ. Microfilms No. 7900125, 117p., 1978.

Two psychoeducational procedures for treating impulsivity in hyperactive children were comparatively evaluated in children both receiving and not receiving stimulant drug therapy. One

hundred twenty hyperactive children at two age levels were assigned to cells in a factorial design wherein the factors were age, drug therapy condition, and psychoeducational treatment. Dependent variables were the scores obtained from Kagan's Matching Familiar Figures Test, the coding subtest of the WISC-R, and a school related copying task both 1 week post-treatment and at a 7 week followup. Results indicate that direct instructional strategies are more likely to be of value in ameliorating impulsive responding than are modeling strategies for both older and younger groups of hyperactive children. Children without drug therapy performed significantly better than those children treated with stimulant drugs. (Journal abstract modified)

002152 Browne, Thomas R. Department of Neurology, Veterans Administration Medical Center, 150 S. Huntington Ave., Boston, MA 02130 **Valproic acid.** New England Journal of Medicine. 302(12):661-666, 1980.

The mechanisms of action, indications, and toxicity of valproic acid (VPA), an antiepileptic drug for the treatment of absence seizures, are described. VPA has been found to be superior to placebo in the treatment of absence (petit mal) seizures, but results for other seizure types have been discouraging. Side-effects of VPA include anorexia, nausea, vomiting, sedation, hepatic toxicity, inhibition of blood coagulation, and teratogenesis. The absorption, distribution, biotransformation, and excretion of VPA are described. Therapeutic plasma concentrations and dosages are noted. 40 references.

002153 Bruni, J.; Wilder, B. J.; Bauman, A. W.; Willmore, L. J. Wilder: Neurology Service, Veterans Administration Medical Center, Gainesville, FL 32602 **Clinical efficacy and long-term effects of valproic acid therapy on spike-and-wave discharges.** Neurology. 30(1):42-46, 1980.

The clinical efficacy and long-term effects of valproic acid therapy on spike and wave discharges were investigated during a 1 year study of 22 patients with absence seizures and other seizure types. Therapeutic results were excellent, with more than 75% improvement in 80% of patients with absence seizures, in 40% of those with tonic/clonic seizures, in all of those with myoclonic seizures, and in 43% of those with partial seizures. Fifty-seven percent of the patients had more than a 75% reduction in the total number of paroxysmal spike wave discharges, and 62% had more than a 75% reduction in the number of spike wave discharges lasting longer than 3 seconds. Photosensitivity and activation by hyperventilation decreased. More patients achieved good EEG control in 1 year than in 10 weeks. 15 references. (Author abstract modified)

002154 Bruni, J.; Wilder, B. J.; Perchalski, R. J.; Hammond, E. J.; Villarreal, H. J. Neurology Service (127), Veterans Administration Medical Center, Gainesville, FL 32602 **Valproic acid and plasma levels of phenobarbital.** Neurology. 30(1):94-97, 1980.

A metabolic study of the concurrent administration of phenobarbital and valproic acid, in which the effects of valproic acid administration on phenobarbital plasma concentrations were investigated, is described. In normal cats and patients with epilepsy, no evidence of decreased renal excretion of phenobarbital was found, despite elevated phenobarbital plasma levels. Metabolic studies in four patients with seizure disorders revealed a decrease in the conversion of phenobarbital to hydroxyphenylphenobarbital and decreased urinary ratios of hydroxyphenobarbital to phenobarbital. These data suggest that phenobarbital metabolism is inhibited by therapeutic plasma levels of valproic acid. 21 references. (Author abstract modified)

002155 Bugiani, Orso; Gatti, Rosanna. Clinica Neurologica, via de Toni 5, I-16132 Genoa, Italy **L-dopa in children with progressive neurological disorders.** Annals of Neurology. 7(1):93, 1980.

The cases of two children with fluctuating dystonic conditions whose neurological pictures were dramatically improved by oral L-dopa administration are presented. Neither complained of parkinsonian symptoms or showed distinct diurnal fluctuations in their disability. When placed on L-dopa therapy (60 to 125mg daily), both children in a few hours gained normal postural mechanisms, gait, and coordination. In one patient, hypotonia was unchanged, while in the other, spasticity was relieved. The positive effect of the therapy could be appreciated whenever L-dopa was discontinued. It is concluded that these cases help to outline the clinical features of a neurological disorder of childhood which is peculiar for its prompt response to L-dopa. 4 references.

002156 Burns, M. E. Lennox Castle Hospital, Glasgow, Scotland **Droperidol in the management of hyperactivity, self-mutilation and aggression in mentally handicapped patients.** *Journal of International Medical Research.* 8(1):31-33, 1980.

The efficacy of long-term oral droperidol treatment for hyperactivity, self-mutilation, aggression, and temper tantrums was investigated using case history data from 16 mentally retarded patients. Behavioral disorders were improved in six patients and were greatly improved in four patients. Two patients experienced accompanying marked beneficial personality changes. In all but two Ss, Parkinsonian side-effects were prevented by the concomitant administration of orphenadrine or benzhexol. 4 references. (Author abstract modified)

002157 Carlsson, Carl; Gullberg, B.; Hostery, U.; Christensson, E. Jarntorgsgatan 8, S-41301 Goteborg, Sweden **A double-blind study of melperone and placebo in hospitalized chronic alcoholics in postintoxication phase.** *International Journal of Clinical Pharmacology and Biopharmacy.* 17(8):341-345, 1979.

A more refined evaluation method of comparing different rating scales and a more precisely defined group of patients were employed to replicate results of a previous study of significant effects of melperone on the symptom of craving in chronic alcoholics. In a double-blind study in chronic alcoholics, melperone was shown to significantly improve muscular and nervous tension, emotional lability, somatization, ability to sleep, anxiety, depression, paranoid ideation, and presumed ability to work, but had no effect on alcoholic craving. The results obtained from three rating scales and the theoretical aspects of alcoholism are discussed. 38 references. (Author abstract modified)

002158 Casey, Daniel E.; Hammerstad, John P. Dept. of Psychiatry, Veterans Administration Hospital, Portland, OR 97207 **Sodium valproate in tardive dyskinesia.** *Journal of Clinical Psychiatry.* 40(11):483-485, 1979.

Effectiveness of sodium valproate in the treatment of neuroleptic-induced tardive dyskinesia (TD) was examined in a 63-year-old male with TD of 2 years duration. Sodium valproate moderately reduced TD with doses of 900 to 3000mg/day, as measured by a tremorograph and rating scales. There was no correlation between dosage, blood levels, or clinical response. Although symptoms were not completely controlled, valproate and other GABAergic agents may be useful compounds in studying and treating TD. 18 references. (Author abstract modified)

002159 Charles, Linda; Schain, Richard J.; Zelniker, Tamar; Guthrie, Donald. Schrain: Dept. of Pediatrics, University of California School of Medicine, Los Angeles, CA 90024 **Effects of methylphenidate on hyperactive children's ability to sustain attention.** *Pediatrics.* 64(4):412-418, 1979.

The attentional characteristics of hyperactive children, the relationship of subjective and objective measures of these characteristics, and the effects of methylphenidate on these measures of attention were investigated in 45 hyperactive children, 6 to 10 years old. Measures included rating scales completed by teachers and parents and a vigilance task. All measures reflected significant changes. Attention and behavior were significantly improved under drug conditions and significantly worsened when methylphenidate was discontinued. However, only performance on the objective measure returned to predrug levels; final off drug parent and teacher ratings remained improved over initial reports. Parent ratings of behavior were unrelated to equivalent teacher ratings. Teachers' ratings of attention correlated with performance on the vigilance task, discriminated between on drug and off drug conditions, and discriminated between children who obtained normal or near normal predrug scores on the objective measure and those who performed poorly. Methylphenidate improved attentional performance for children who had poor predrug scores on the vigilance task, but did not produce a significant change on the scores of children with normal predrug performance. 21 references. (Author abstract)

002160 Charles, Linda; Schain, Richard J.; Guthrie, D. Dept. of Pediatrics, University of California School of Medicine, Center for the Health Sciences, Los Angeles, CA 90024 **Long-term use and discontinuation of methylphenidate with hyperactive children.** *Developmental Medicine and Child Neurology.* 21(6):758-764, 1979.

The long-term effects of methylphenidate on the behavior and academic functioning of hyperactive children are described. Thirty-six children having a positive response to methylphenidate entered a 3 year followup study in which they were closely monitored physically, behaviorally, and psychometrically. During this period, 13 children spontaneously discontinued medication; there were no statistically significant differences between them and the children who continued medication in terms of age, IQ, or ratings at initial interview. The greatest improvement in performance occurred in the early months of treatment, but was only partially maintained during long-term therapy and little further change occurred after medication was discontinued. Findings indicate that sustained improvement is related to factors other than continued medication, and they suggest that drug therapy should be regarded as a short-term intervention until more positive social and school behavior can be established. 13 references. (Author abstract)

002161 Childress, Robert Ney. Texas Tech University **The effectiveness of EMG biofeedback training compared to Ritalin (methylphenidate) in the management of hyperkinesis. (Ph.D. dissertation).** *Dissertation Abstracts International.* 40(2):906-B, 1979. Ann Arbor, Univ. Microfilms No. 7917313, 256p., 1978.

The comparative effectiveness of electromyographic biofeedback (EMG/BF) and methylphenidate (Ritalin) in the management of hyperkinesis was assessed in 28 physician diagnosed hyperkinetic children with established Ritalin medication regimens. Three to six independent measures were used to assess each of six basic problem areas characteristic of the hyperkinetic syndrome: 1) motor behavior, 2) attention/perception, 3) learning, 4) impulse control, 5) interpersonal relationships, and 6) emotionality. Although both treatments produced consistently significant improvement, there was clear evidence of the superiority of Ritalin over EMG/BF in only one area (motor behavior improvement). (Journal abstract modified)

002162 Cloyd, James C.; Wright, Ballard D.; Perrier, Donald. College of Pharmacy, University of Minnesota, Minneapolis, MN 55455 **Pharmacokinetic properties of thiopental in two pa-**

tics treated for uncontrollable seizures. *Epilepsia*. 20(3):313-318, 1979.

Thiopental was administered for seizure control in 2 patients with uncontrollable seizures. Serum samples were collected from each patient and assayed for thiopental, and the resulting serum concentrations/time data were analyzed pharmacokinetically. The biologic half-life in both patients was significantly longer than previously reported values. Based on the limited number of patients studied, it would appear that half-life and volume of distribution increase with the degree of obesity, while clearance remains unchanged. These pharmacokinetic characteristics would be worthy of consideration in cases where there may be prolonged use of thiopental, e.g., for the control of uncontrollable seizures. 10 references. (Author abstract)

002163 Congdon, P. J.; Forsythe, W. I. St. James's University Hospital, Leeds LS1 3EX, England **Intravenous clonazepam in the treatment of status epilepticus in children.** *Epilepsia*. 21(1):97-102, 1980.

The treatment of 17 children (age range 2 weeks to 15 years) who developed status epilepticus with intravenous clonazepam (Rivotril) is described. Status was promptly stopped in each instance with between 0.25 to 0.75mg/kg clonazepam. In six children who had a further episode of status epilepticus, diazepam (0.25 to 0.75mg/kg) was given. A comparison of their relative efficacy indicated that in each case clonazepam had a more prolonged action. No serious side-effects occurred. It is recommended that clonazepam, because of its more prolonged action, be the drug of choice in controlling status epilepticus. 20 references. (Author abstract modified)

002164 Coulam, Carolyn B.; Annegers, John F. Mayo Clinic, Rochester, MN 55901 **Do anticonvulsants reduce the efficacy of oral contraceptives?** *Epilepsia*. 20(5):519-525, 1979.

An investigation of 82 patients taking oral contraceptives and anticonvulsants of whom 41 had used both medications for a total of 955 months is reported. Three documented oral contraceptive failures occurred during this period, whereas the expected number was 0.12. No pill failures were observed in 2,278 months among women with epilepsy who were taking oral contraceptives but were not taking anticonvulsants at this time. It is suggested that there is an increased rate of pill failure among women taking anticonvulsants and that the advisability of using oral contraceptives when anticonvulsant medication is being used may need to be evaluated. 25 references. (Author abstract modified)

002165 Cowley, Luis M.; Glen, Robert S. P.O. Box 70, Terrell, TX 75160 **Double-blind study of thioridazine and haloperidol in geriatric patients with a psychosis associated with organic brain syndrome.** *Journal of Clinical Psychiatry*. 40(10):411-413, 416-419, 1979.

The efficacy and safety of thioridazine and haloperidol in the treatment of psychosis associated with organic brain syndrome in the elderly were investigated in a 12 week double-blind study using 40 geriatric patients from a psychiatric ward of a state hospital. Two types of patients comprised the population, those who had been hospitalized most of their adult lives and those who had not entered the hospital until late in life. Although both drugs produced significant improvement in these patients' symptoms, the improvement with thioridazine tended to be greater than that with haloperidol in most ratings. A plateau effect was seen with haloperidol in contrast to a steady improvement seen with thioridazine. The safety of both drugs was confirmed. Geriatric patients who display both psychotic and organic brain syndrome symptomatology were found to respond quite well to both drugs, regardless of their previous psychiatric

history, but a somewhat more dramatic response was seen with thioridazine. 14 references. (Author abstract modified)

002166 Craggs, M. D.; Wright, J. J.; Werry, J. S. Dept. of Psychiatry, School of Medicine, University of Auckland, Auckland, New Zealand **A pilot study of the effects of methylphenidate on the vigilance-related EEG in hyperactivity.** *Electroencephalography and Clinical Neurophysiology*. 48(1):34-42, 1980.

The effects of methylphenidate on reaction time (RT) and EEG were examined in seven hyperactive boys between 8 and 12 years of age. Methylphenidate reduced RT on a test requiring prolonged vigilance, but increased EEG alpha power relative to higher and lower frequencies in five of the Ss. RT increased during the course of the task and relative EEG alpha power increased compared to other frequencies. The RTs showed an even greater increase with prolonged vigilance when the Ss were off medication, but the accompanying EEG changes were the opposite of those seen on medication. The EEG of these hyperactive children was closer to normal under methylphenidate than under the nonmedicated condition. 21 references.

002167 Creedon, Michael A. University of Maryland Baltimore Professional Schools **Social and organizational influences on the use of psychotropic drugs in nursing homes.** (D.S.W. dissertation). Dissertation Abstracts International. 40(8):4746-A, 1980. Ann Arbor, Univ. Microfilms No. 8003096, 168p., 1979.

The influence of organizational, social, and technical characteristics of nursing homes on the use of psychotropic drugs for residents was examined. Twenty nursing homes were investigated and 597 residents of the nursing homes were analyzed for drug use patterns. The findings support the hypotheses that: psychotropic drug use is influenced by other organizational characteristics, and social interaction may be viewed as an alternative technique of care for such drugs for at least a proportion of nursing home residents. Recommendations are made to reduce the psychotropic drug use in nursing homes. (Journal abstract modified)

002168 Dall, John L. C. Victoria Geriatric Unit, Glasgow, Scotland **Chlormethiazole and electroencephalogram changes.** *Age and Ageing*. 8(4):268-271, 1979.

The use of EEGs in the assessment of the therapeutic effect of chlormethiazole (Heminevrin) and chlorpromazine (Largactil) in a group of patients with moderately severe chronic brain failure is described. A cross-over trial was carried out with an initial titration period of 2 weeks, a treatment period of 2 weeks with drug A, followed by a washout period of 1 week, and then a titration period of 2 weeks with drug B, followed by a final treatment period of 2 weeks. Observations were also made on the EEG before starting therapy, and during the treatment period with each drug, giving three records for comparison. Nine patients were thought to be better on chlormethiazole. Of the other seven patients, four were improved on chlorpromazine while in the remainder there was either no significant difference between the control observations and the observations on treatment, or both treatment regimes resulted in equal improvement giving a net observation of 0 on the graph (three cases). Observations of EEG changes showed good correlation with clinical observation in assessing regimes in nine cases and fair correlation in a further five.

002169 Dam, Mogens; Christiansen, J.; Munck, O.; Mygind, K. I. University Clinic of Neurology, Hvidovre Hospital, DK-2650 Hvidovre, Denmark **Antiepileptic drugs: metabolism in pregnancy.** *Clinical Pharmacokinetics*. 4(1):53-62, 1979.

In an open prospective clinical study, plasma clearance of phenytoin, phenobarbital, and carbamazepine was assessed in 14 epileptic patients during and after pregnancy. Plasma clearance showed a marked increase during pregnancy, reached a maximum just before or after delivery, and then decreased to early pregnancy values. The relative plasma concentration of carbamazepine-10,11-epoxide to that of carbamazepine increased similarly during pregnancy. The protein binding of carbamazepine and the epoxide was not influenced by pregnancy. A higher rate of hepatic drug metabolism, due to alteration of the physiological state in pregnancy is suggested as the most reasonable explanation. No change in seizure frequency was observed, probably because of frequent dose adjustments to maintain optimal plasma levels. 25 references. (Author abstract)

002170 Danjoux, J.; Moron, P. Moron: Service medico-psychologique, Hotel-Dieu, F-31052 Toulouse Cedex, France /On the effect of an inhibition counteracting drug in the adolescent./ De l'action d'un desinhibiteur chez l'adolescent. *Neuropsychiatrie de l'Enfance et de l'Adolescence*. 27(6):293-297, 1979.

The therapeutic effects of caripramine were studied in an adolescent population. Ss were 23 adolescents (ages 14 to 18) presenting with depression, anxiety, and inhibition. Between 100 and 200mg of caripramine were administered daily. The average length of treatment was approximately 45 days. In more than half the cases, improvement was noted before the second day of treatment. The drug had an inhibition counteracting and psychostimulatory effect and was shown to be capable of raising the activity level and improving the mood of the treated Ss. 34 references.

002171 DeFreitas, Brian; Schwartz, George. Douglas Hospital Centre, 6875 LaSalle Blvd., Montreal, Quebec H4H 1R3, Canada Effects of caffeine in chronic psychiatric patients. *American Journal of Psychiatry*. 136(10):1337-1338, 1979.

The question whether the reduction or elimination of caffeine intake would affect the behavior of chronic psychiatric patients was investigated. The Brief Psychiatric Rating Scale (BPRS) was completed by each of 14 patients before and at the end of the baseline decaffeinated coffee period. Analysis of variance of the BPRS revealed significant changes on the total score, the hostile suspiciousness factor, and the items measuring somatic concern, anxiety, tension, hostility, and excitement. Thus, results indicate a general improvement in patients whose caffeine intake had been reduced. This improvement was reversed when regular coffee was reintroduced. The findings bring into question the practice of indiscriminately giving caffeinated products to patients in psychiatric hospitals. 4 references.

002172 Dowrick, Peter W. Dept. of Psychiatry, School of Medicine, University of Auckland, P.B., Auckland, New Zealand Single dose medication to create a self model film. *Child Behavior Therapy*. 1(2):193-198, 1979.

An example of videotaped self-modeling which capitalizes in an unusual way on the effects of a single dose of medication is presented. A single dose of diazepam induced clearly observable one time changes in a socially withdrawn 5-year-old boy. These behaviors were captured on videotape and subsequently replayed to the S for successful therapeutic self-modeling. Multiple baseline data suggest that neither medication nor self-modeling alone would have been sufficient for lasting changes in verbal behavior. This unusual combination of procedures requires further research into its application in other situations. 6 references. (Author abstract)

002173 Eadie, M. J. Dept. of Medicine, University of Queensland, Brisbane, Queensland, Australia Epilepsy in pregnancy: the

need for effective treatment. *Current Therapeutics*. 20(4):11-13, 1979.

The effect of epilepsy and its treatment on pregnancy is discussed. A number of recent studies have indicated that epilepsy tends to worsen during pregnancy, possibly as a result of the tendency for plasma concentrations of anticonvulsant to fall as pregnancy progresses. The etiology of this fall in plasma anticonvulsant levels is likely to be multifactorial. To maintain therapeutic plasma drug levels, drug doses must be adjusted and careful monitoring both during and after pregnancy is recommended. Evidence for dysmorphogenesis have been found both in offspring of epileptic mothers receiving anticonvulsants and in offspring of epileptic fathers, suggesting that the epilepsy itself may contribute to increased infant risk. Anticonvulsant-induced neonatal bleeding is preventable. While parental epilepsy may be a disadvantage for the fetus, the need to prescribe anticonvulsants during pregnancy may not necessarily increase that disadvantage. 8 references.

002174 Egan, Rosemary Whittle. Saint Louis University Research variables in CNS stimulant studies. (Ph.D. dissertation). Dissertation Abstracts International. 39(10):6061-A, 1979. Ann Arbor, Univ. Microfilms No. 7908268, 155p., 1978.

A review of the research variables used in studies of the five CNS stimulants (Benzedrine, Cylert, Deanol, Dexedrine, and Ritalin) is presented. A thorough search of the literature yielded 48 studies; these were evaluated in light of the revised Campbell and Stanley (1963) framework for evaluating internal and external validity. Evidence supports the conceptual hypothesis that environmental and maturational factors modify the effect of a drug on a given child and that these factors have not been controlled. It is concluded that factors in four major areas (sample selection, research design, measurement techniques, and individualized medical supervision) need to be controlled in future drug research. (Journal abstract modified)

002175 Evans, M. A.; Triggs, E. J.; Broe, G. A.; Saines, N. Triggs: Dept. of Pharmacy, University of Sydney, Sydney, New South Wales 2006, Australia Systemic availability of orally administered L-dopa in the elderly Parkinsonian patient. *European Journal of Clinical Pharmacology*. 17(3):215-221, 1980.

The systemic availability of orally administered L-dopa in five elderly Parkinsonian patients was investigated and compared to that of six young, healthy volunteers following a single oral 300mg dose. Quantitation of plasma levels of intact L-dopa was effected by ion exchange column chromatography and spectrofluorimetry. The L-dopa plasma concentration time profiles obtained confirmed the considerable intersubject variability in the absorption of L-dopa previously reported in the literature. Maximum plasma concentrations of L-dopa generally occurred within 60 minutes of administration of the dose. The existence of more than one plasma peak of L-dopa concentration was displayed in 45% of Ss studied. This characteristic was not confined exclusively to either S group. There was a significantly larger area under the plasma L-dopa concentration time curve in the elderly Parkinsonian patients compared to the young, healthy volunteer Ss. A significant correlation existed between area under the plasma L-dopa concentration time curve and age among the Ss. The apparent elimination phase plasma half-life of L-dopa in the elderly Parkinsonian patients was not significantly different from that observed in the young, healthy volunteers. These results suggest that there may be an age related alteration to the disposition of orally administered L-dopa in the elderly Parkinsonian patient. 27 references. (Author abstract modified)

002176 Evans, Richard; Di Scipio, William. Bronx Children's Psychiatric Center, 1000 Water Place, Bronx, NY 10461 Non-

pharmacologic factors in the administration of p.r.n. psychotropic medication on an adolescent unit. *American Journal of Psychiatry.* 137(1):123-124, 1980.

Nonpharmacologic factors involved in the administration of p.r.n. psychotropic medication to adolescents in a children's psychiatric center were examined. Data analyzed for a 1 year period included time of administration, medication and dose, route of administration, nurse's name, patient's name, maintenance medication, patient's duration of stay, and whether p.r.n. dose was given to one individual or more than one within 5 minutes. The results indicate that approximately 30% of p.r.n. doses exert their primary effect pharmacologically, while the remaining 70% worked primarily through nonpharmacologic factors. Among those factors were time of day, familiarity of both staff and patients with the institution, positive expectations for the medication, and a contagion effect whereby nurse and patient acted together in order to resolve an escalating crisis. An increasing reliance upon the positive placebo effect was seen. It is concluded that this reliance led to reduced attempts at other management approaches that have potential for teaching self-regulation. 9 references.

002177 Felthous, Alan R.; Robinson, David B.; Conroy, Robert W. Menninger Foundation, Box 829, Topeka, KS 66601 **Prevention of recurrent menstrual psychosis by an oral contraceptive.** *American Journal of Psychiatry.* 137(2):245-246, 1980.

Evidence is presented on the effectiveness of oral contraceptives in preventing the recurrence of menstrual psychosis, a disorder thought to be related to fluctuating levels of sex steroid hormones. A 21-year-old woman was treated with a contraceptive after treatment with chlorpromazine and haloperidol had no effect on her psychotic symptoms, which appeared and disappeared during the menses. The possible mechanism of action of the contraceptive is proposed, implicating the role of monoamine oxidase activity and brain neurotransmitters. 5 references.

002178 Fletcher, Constance Neil. Illinois Institute of Technology **The effects of thioridazine withdrawal on the physical, social, cognitive and self care functioning of severely and profoundly retarded children.** (Ph.D. dissertation). Dissertation Abstracts International. 39(8):4088-B, 1979. Ann Arbor, Univ. Microfilms No. 7902989, 67p., 1978.

The effects of the use and withdrawal of thioridazine on a variety of behaviors was examined in an institutionalized population of severely retarded children. Variables measured included self-help skills, problem behavior, drug side-effects, and learning potential. Statistical analysis of results yielded no significant differences between groups during a baseline period or during treatment in which one half of the children were randomly withdrawn from the drug. Results indicate a lack of documented benefits of drug use at the time of the study. Questions and concerns regarding implications of findings are raised, and areas for future study are suggested. (Journal abstract modified)

002179 Forsythe, W. I.; Prendergast, M. P.; Toothill, C.; Broughton, P. M. G. Paediatric Department, Leeds General Infirmary, Great George Street, Leeds 1, England **Carbamazepine serum levels in children with epilepsy: a micro immuno-assay technique.** *Developmental Medicine and Child Neurology.* 21(4):441-447, 1979.

A group of children with seizures were given carbamazepine, and data were obtained on side-effects and drug effectiveness. Equilibrium was reached within 4 to 6 days in 25 of 26 Ss with a dosage of 20mg/kg/day. The sudden withdrawal of other anticonvulsants did not usually affect the rise of carbamazepine in serum unless given in high doses. Satisfactory levels were obtained in the serum of 38 children given the drug either twice or

three times daily, but higher levels were obtained with the latter. The lowest serum level associated with complete seizure control was 6mg/l. Seizure control was comparable whether carbamazepine was given twice or three times daily. Complete control of temporal lobe seizures was obtained in nine of 20 Ss and of grand-mal in 10 of 18 Ss. Carbamazepine serum levels remained remarkably constant during a 10 to 30 month followup. 10 references. (Author abstract modified)

002180 Forsythe, W. I.; Prendergast, M. P.; Toothill, C.; Broughton, P. M. G. Paediatric Department, Leeds General Infirmary, Great George Street, Leeds 1, England **Phenytoin serum levels in children with epilepsy: a micro immuno-assay technique.** *Developmental Medicine and Child Neurology.* 21(4):448-454, 1979.

The enzyme multiple immunoassay technique was used to study phenytoin serum levels in 50 children with seizures. It was found that: 1) a 5mg/kg/day single dose in suspension or capsules produced inadequate serum levels 16 and 24 hr after ingestion; 2) twice daily dosages produced adequate serum level in most children; 3) 12 Ss continued to have seizures, but six achieved control at 10mg/kg/day; 4) phenytoin reached equilibrium in the serum within 5 days provided phenobarbitone had not been previously provided; 5) phenytoin suspension given twice daily produced satisfactory serum levels provided the bottle was shaken well before dispensing; and 6) apart from minor variations, phenytoin maintained its level in serum during a 14 to 30 month followup period, whether 5mg or 10mg/kg/day was given. 12 references. (Author abstract modified)

002181 Freeman, Richard J. University of Waterloo (Canada) **The effects of methylphenidate on avoidance learning and risk-taking by hyperkinetic children.** (Ph.D. dissertation). Dissertation Abstracts International. 39(9):4576-B, 1979. (Not available from Univ. Microfilms), 1978.

The effects of methylphenidate on avoidance learning and risk-taking by hyperkinetic children were examined. On the basis of three studies, it is concluded that the behavior of hyperkinetic children who show favorable clinical response to methylphenidate is relatively resistant to control by primary noxious contingencies, but that their behavior is made more normal by the administration of methylphenidate. The results are discussed in terms of a model of impulsiveness which is outlined. A parallel is drawn between the behavior of hyperkinetic children and that seen in other disorders of impulse control, particularly psychopathy. The proposition is advanced that a relationship may exist between childhood hyperkinesis and psychopathology, and the implications of such a link are discussed. (Journal abstract modified)

002182 Frost, James D., Jr.; DeLucchi, Milton R. Dept. of Neurology, Baylor College of Medicine, 1200 Moursund Ave., Houston, TX 77030 **Insomnia in the elderly: treatment with flurazepam hydrochloride.** *Journal of the American Geriatrics Society.* 27(12):541-546, 1979.

Under sleep laboratory control, the efficacy of flurazepam hydrochloride was evaluated in six women with objectively verified insomnia. Sleep records obtained during 3 placebo baseline nights, consecutive flurazepam nights, and 3 placebo withdrawal nights were evaluated by means of electroencephalographic, electrooculographic, and electromyographic criteria. A reduction in sleep latency and total awake time and a corresponding increase in total sleep time were demonstrated during the active drug period. No evidence of diminishing effectiveness was observed during the 7 days of drug administration. It is concluded that flurazepam HCl, administered in 15mg dosage for a period of 7 nights, appears to be effective for the temporary amelioration

tion of insomnia in six geriatric women. 10 references. (Author abstract modified)

002183 Gimenez-Roldan, S.; Martin, M. Dept. of Neurology, Ciudad Sanitaria Provincial, Madrid, Spain **Effectiveness of clonazepam in startle-induced seizures.** *Epilepsia*. 20(5):555-561, 1979.

The effectiveness of clonazepam in startle-induced seizures is described. Five cerebral palsied children and adolescents with severe startle epilepsy became seizure free after clonazepam was introduced into their existing anticonvulsant drug regimens, although the drug was withdrawn in one case because of side-effects. Two hemiparetic patients who had startle epilepsy as the only epileptic manifestation remained permanently controlled after a mean of 34 months of continuous therapy. Reappearance of startle-induced seizures occurred after 1 and 4 years in two other patients with the Lennox-Gastaut syndrome. Possible mechanisms of clonazepam in this form of reflex epilepsy are discussed. 21 references. (Author abstract modified)

002184 Gittelman, Martin. Dept. of Psychiatry, New Jersey Medical School, 100 Bergen St., Newark, NJ 07103 **Refining diagnosis and behavioral intervention: key to preventing overmedication.** *International Journal of Mental Health*. 8(1):3-9, 1979.

Management of childhood hyperactivity is explored focusing on prevention of overmedication. It is argued that the diagnosis of hyperactivity tends to encompass far too much, and that drugs, which can be effective, are used too often and for too long, without close continuing contact between parent, school, and prescribing physician. It is recommended that in most cases, simple assistance by the child's teacher and parents, often under professional guidance, will be effective. If this is not enough, it is suggested that the nature of a child's disorders should be delineated precisely and a list of prescriptive habilitative measures be developed. Limitations on the use of drugs to treat hyperactivity are noted. 7 references.

002185 Gold, Mark S.; Pottash, A. Carter; Sweeney, Donald R.; Kleber, Herbert D. Research Facilities, Fair Oaks Hospital, 19 Prospect St., Summit, NJ 07901 **Opiate withdrawal using clonidine: a safe, effective, and rapid nonopiate treatment.** *Journal of the American Medical Association*. 243(4):343-346, 1980.

Clonidine hydrochloride was administered to 10 patients in an inpatient setting after abrupt discontinuation of chronic methadone hydrochloride administration. Clonidine produced a rapid and statistically significant decrease in opiate withdrawal signs and symptoms. Clonidine administration for 14 days enabled all patients to be successfully detoxified from chronic opiate administration. In all patients studied, clonidine was a safe and effective nonopiate treatment of opiate withdrawal. These data support the hypothesis that the alpha2-adrenergic agonist, clonidine, has substantial antiwithdrawal effect by replacing opiate mediated inhibition with alpha2-mediated inhibition of brain noradrenergic activity. 20 references. (Author abstract)

002186 Goldstein, Stanley E.; Birnbaum, Frances. Queensway-Carlton Hospital, 3045 Baseline Road, Ottawa, Ontario, Canada L2H 8P4 **Nylidrin HCl in the treatment of symptoms of the aged: a double-blind placebo controlled study.** *Journal of Clinical Psychiatry*. 40(12):520-524, 1979.

The effectiveness and safety of nylidrin HCl were investigated in a geriatric population (n=60) with mild to moderate symptoms of cognitive, emotional, and physical impairment and a primary diagnosis of nonpsychotic organic brain syndrome. Following a 3 week placebo washout, patients received either nylidrin HCl or placebo for 12 weeks. Efficacy evaluations were made utilizing the Sandoz Clinical Assessment Geriatric Scale, a nurse rating of ward behavior, the Hamilton Psychiatric

Rating Scale for Depression, and two of the Katz Adjustment Scales. Significant improvement in symptom severity was demonstrated in the nylidrin group as compared to the placebo group. There were no abnormalities of clinical significance in the safety measurements, and few side-effects were reported. 10 references. (Author abstract modified)

002187 Gram, Lennart; Flachs, Helga; Wurtz-Jorgensen, Anne-lise; Parnas, Josef; Andersen, Bjorn. Epilepsy Dept., Filadelfia Colony, Dianalund, Denmark **Sodium valproate, serum level and clinical effect in epilepsy: a controlled study.** *Epilepsia*. 20(3):303-311, 1979.

Clinical effects at three different serum levels of sodium valproate (VPA) were compared in a triple-blind, multiple cross-over trial comprising 13 epileptic inpatients. Patients were selected regardless of seizure type, and all were in concomitant antiepileptic treatment, which was kept constant throughout the study. A significant relationship between the decrease in number of seizures and increasing VPA serum level was demonstrated. The relationship between VPA dose and serum level was curvilinear. Statistical evaluation of patients by seizure type in relation to clinical effect of VPA was only possible for secondary generalized seizures. Between phenytoin, phenobarbital, and carbamazepine and the different VPA serum levels no interactions could be demonstrated. Recorded side-effects were always mild and transient. No obvious correlation between side-effects and VPA serum level was established. 27 references. (Author abstract)

002188 Graux, P.; Durocher, A.-M. Hopital Swynghedam, F-59037 Lille Cedex, France **Parkinson's disease in the elderly./ Une personne agee parkinsonienne.** *Revue de Geriatrie*. 4(8):415-417, 1979.

Treatment of elderly patients suffering from Parkinson's disease in France is discussed. The prescription, secondary effects, and the results of the use of Levodopa are described. Since the drug causes complications in some cases, other medications are used, such as Parlodel (bromocriptine), Trivastal (piribedil), and Mantadix (amantadine hydrochloride). Treatment of the initial stage and of complicated forms is also discussed. Physioathological and etiological data on the Parkinson syndromes are also given.

002189 Gray, J. A. Dept. of Experimental Psychology, South Parks Road, Oxford OX1 3UD, England **Anxiety and the brain: not by neurochemistry alone.** *Psychological Medicine*. 9(4):605-609, 1979.

The importance of the recent discovery of receptors in the central nervous system that specifically bind benzodiazepines is discussed. This discovery is seen as a clue that will direct researchers to the areas of the brain on which anti-anxiety drugs act. However, it is noted that benzodiazepines are more than simple anti-anxiety drugs. The question of what synaptic and neural events intervene between the binding of the benzodiazepines to their receptor and the action which they exert on the septohippocampal system is addressed. 42 references.

002190 Guareschi-Cazzullo, A.; Bertolini, M. Institute Children's Psychiatry, University of Milan, Via G. F. Besta, 1, I-20161, Milan, Italy **Psychopharmacological perspectives in childhood psychoses.** *Progress in Neuro-Psychopharmacology*. 3(1-3):53-58, 1979.

Psychopharmacological perspectives in childhood psychoses are presented, and the use of antidepressive drugs in the childhood psychoses is reviewed. It is contended that antidepressive drugs, either alone or associated with neuroleptics, have shown great promise in the childhood psychoses, even when depressive

symptoms are not clearly evident. The following aspects of childhood depression are discussed: psychopathological features from the psychodynamic point of view, neurofunctional background in various ages, pharmacodynamic characteristics of drugs, lithium treatment, and biochemical markers in endogenous depression. 22 references. (Author abstract modified)

002191 Guarnieri, M.; Placidi, G. F.; Cassano, G. B. Psychiatry Institute, University of Pisa, Pisa, Italy **Depot neuroleptics in the treatment of acute psychoses.** *Encephale*. 5(2):189-193, 1979.

Data derived from clinical records of 43 acute inpatients treated with the depot neuroleptic fluphenazine decanoate (F.D.) during a 1 year period are presented. The records are from patients showing acute symptomatology of the schizophrenic, schizoaffective, or manic type whose clinical characteristics did not represent an indication for long-term treatment to be maintained after the episode. With such treatment it was possible to eliminate the stressful forced repeated drug administrations without any particular side-effects and the drug combinations were greatly reduced. It is noted, however, that clinical observations in this study need further confirmation. 11 references. (Author abstract modified)

002192 Hoehn, Margaret M. Box A035, University of Colorado Medical Center, 4200 E Ninth Ave., Denver, CO 80262 **Increased dosage of carbidopa in patients with Parkinson's disease receiving low doses of levodopa: a pilot study.** *Archives of Neurology*. 37(3):146-149, 1980.

Twenty-one patients with Parkinson's disease were studied because their low maintenance dosages of carbidopa: levodopa in the customary ration of 1:10 provided less than the daily 75mg of carbidopa believed necessary to achieve full inhibition of extracerebral dopa decarboxylation. The dosage of carbidopa was increased 2.5 times to between 75 and 150mg daily, while the mean dosage of levodopa essentially was unchanged. The new carbidopa: levodopa ratio was 1:4. During 15 months, this treatment produced a moderate decrease in the severity of parkinsonism and a marked decrease in peripheral adverse reactions without a significant increase in the central adverse effects of levodopa. It is concluded that increasing the dosage of carbidopa may be beneficial to patients with Parkinson's disease receiving less than 75mg of carbidopa and 750mg of levodopa daily. 8 references. (Author abstract modified)

002193 Hoes, M. J. A. J. M. Bethesda Hospital, NL-4000 AA Tiel, The Netherlands **Coppersulphate and pimozone for anorexia nervosa.** *Journal of Orthomolecular Psychiatry*. 9(1):48-51, 1980.

Homovanillic acid (HVA) and vanillylmandelic acid (VMA) levels prior to and during treatment with copper sulphate and pimozone were examined in eight females meeting criteria for anorexia nervosa. Of these, all but one patient previously treated with lyndiol R, showed low serum copper and low urinary HVA and VMA values. After 10 weeks' treatment, all eight patients showed clinical improvement in anorexia nervosa symptomatology, including increased body weight and resumption of menstruation; and all could be discharged from the hospital. Results are discussed in terms of a proposed pathophysiological model of dopaminergic hyperfunctioning and noradrenergic hypofunctioning in anorexia nervosa. In this model, lowered dopamine-beta-hydroxylase activity and a copper deficiency are etiologically important. The beneficial effects of pimozone are disease specific, as on clinical indications, anorexia is described as a side effect of pimozone. Further research is recommended. (Author abstract modified)

002194 Huddad, Fuad Sami; Risk, Winthrop S. Risk: Dept. of Neurology, University of Iowa Hospitals and Clinics, Iowa City, IA 52242 **Isopropinose treatment in 18 patients with sub-**

acute sclerosing panencephalitis: a controlled study. *Annals of Neurology*. 7(2):185-188, 1980.

A controlled clinical trial of isopropinose (inosiplex), a proposed antiviral agent, in 18 patients with subacute sclerosing panencephalitis (SSPE) is described. No great improvement occurred in any patient soon after treatment, but two patients did improve substantially several months after discontinuing isopropinose. Spontaneous improvement also occurred in four out of 96 control Ss. Because of the variable natural history of SSPE, differences in clinical improvement between treated patients and control Ss were not significant. Changes in serial measles antibody titers did not correlate with therapy. 13 references. (Author abstract modified)

002195 Huessy, Hans R.; Blair, Charles L.; Rood, Pamela. Dept. of Psychiatry, Medical Alumni Building, University of Vermont, Burlington, VT 05401 **Pharmacotherapy of adult minimal brain dysfunction.** *Hillside Journal of Clinical Psychiatry*. 1(2):193-205, 1979.

Several drugs which have been successful in controlling symptoms of childhood minimal brain dysfunction were used to treat adults with similar childhood histories and/or symptoms. A group of 64 adult psychiatric patients were given 142 drug trials. Improvement was observed in 48% of the trials, and 77% of the Ss responded favorably to at least one of the drugs. Positive responses were about the same for the three drugs used most frequently: imipramine, methylphenidate, and amitriptyline. Dextroamphetamine, diphenhydantoin, pemoline, and methamphetamine were also included in the trials. 34 references. (Author abstract modified)

002196 Ingall, Michael A.; Farber, Barry L.; Kuppe, Jane V.; Silveira, Anne P. Providence Mental Health Center, Inc., 100 Fountain St., Providence, RI 02903 **Outpatient titration with intramuscular haloperidol as an alternative to psychiatric hospitalization.** *Rhode Island Medical Journal*. 62(11):437-442, 1979.

The outpatient use of rapidly sequential intramuscular doses of haloperidol (titration) in severely agitated patients with acute psychosis is described. Ss present at the emergency service of a community mental health center and this technique has enabled the staff to treat on an outpatient basis a group of highly disturbed patients who have previously required psychiatric hospitalization. 5 references. (Author abstract modified)

002197 Inoue, Youichiro; Imazato, Katsujiro; Arikawa, Katsuyoshi; Inanaga, Kazutoyo; Miura, Tomonobu. Dept. of Neuropsychiatry, School of Medicine, Kurume University, Fukuoka, Japan **Clinical effects of L-dopa on epilepsy.** *Folia Psychiatrica et Neurologica Japonica*. 33(3):307-309, 1979.

The clinical efficacy of L-dopa in the treatment of epilepsy was evaluated in 14 hospitalized chronic epileptic patients with psychiatric symptoms. L-dopa was moderately effective in three cases, slightly effective in six cases, and ineffective in five cases. The seizures decreased slightly in frequency in five cases and moderately in two cases. L-dopa was effective on psychiatric symptoms of epilepsy (lack of activity and spontaneity and dysphoria) in eight cases. EEG data indicate that paroxysmal discharge decreased in frequency in six cases and background activity improved in six cases. 3 references.

002198 Israel, L.; Ohlmann, Th.; Hugonot, R. Hugonot: Service de Geriatrie, C.H.U. de Grenoble, F-38700 La Tronche, France **Effectiveness of vincamine with outpatients: a psychometric double-blind study.** *Efficacite d'une vincamine en ambulatorio: etude psychometrique en double aveugle.* *Revue de Geriatrie*. 4(8):429-433, 1979.

The effectiveness of the drug Vincacor-Retard (vincamine) was tested on 38 subjects 56 to 91 years old: 19 patients were given the drug, and 19 received a placebo. The tests measured vigilance, memory, fluidity, and psychomotor effects. It was found that the group treated with the drug showed a significant improvement of performance as compared to the group using placebo with regard to the most important two factors: vigilance and memory. It is concluded that the results obtained with Vincacor-Retard are significant when the effect of placebo is eliminated. Therefore, it is considered that the results obtained from elderly outpatients are the best obtained so far with regard to medications which have cerebral effects.

002199 Jeste, Dilip V.; Rosenblatt, Jack E.; Wagner, Richard L.; Wyatt, Richard J. National Institute of Mental Health, St. Elizabeths Hospital, Washington, DC 20032 **High serum neuroleptic levels in tardive dyskinesia?** *New England Journal of Medicine*. 301(21):1184, 1979.

The relationship between the daily dose of a neuroleptic and the risk of tardive dyskinesia (TD) was studied with 30 chronically ill elderly female psychiatric inpatients. TD was diagnosed in eight patients who were taking thioridazine or mesoridazine. A control group of eight patients without TD (six taking thioridazine, and two mesoridazine) were matched with the TD group for diagnosis and mean age, height, weight, length of neuroleptic treatment, and score on a behavior rating scale for geriatric inpatients. Five of the eight patients were also matched for present daily dose of the neuroleptic. Blood was collected after patients had been on stable doses of medications for at least a month. Covarying for the daily dose showed that the serum neuroleptic activity was significantly greater in patients with TD than in controls, in both the dose matched subjects and to the total group. Data indicate that there is little clinical evidence of a relation between the daily dose of a neuroleptic and the risk of TD. However, preliminary findings suggest that high concentrations of neuroleptics may contribute to the pathophysiology of TD in at least a subgroup of patients. 4 references.

002200 Jimerson, David C.; Post, Robert M.; Stoddard, F. J.; Gillin, J. C.; Bunney, W. E., Jr. Post: NIH, Building 10, Room 2S239, 9000 Rockville Pike, Bethesda, MD 20205 **Preliminary trial of the noradrenergic agonist clonidine in psychiatric patients.** *Biological Psychiatry*. 15(1):45-57, 1980.

A preliminary double-blind trial of the alpha-adrenergic agonist clonidine, which is widely used in the treatment of hypertension in psychiatric patients is reported. Two schizophrenic patients became more agitated and aggressive during the trial. The drug showed some antidepressant effects in three of five depressed patients. Clonidine withdrawal appeared to potentiate symptoms in a manic patient. Drug treatment reduced blood pressure and REM sleep. Interpretation of behavioral effect of clonidine is limited by uncertainty about the balance of its presynaptic and postsynaptic effects. 82 references. (Author abstract modified)

002201 Johansson, Folke; von Knorring, Lars; Sedvall, Goran; Terenius, Lars. von Knorring: Dept. of Psychiatry, University of Umea, S-90185 Umea, Sweden **Changes in endorphins and 5-hydroxyindoleacetic acid in cerebrospinal fluid as a result of treatment with a serotonin reuptake inhibitor (zimelidine) in chronic pain patients.** *Psychiatry Research*. 2(2):167-172, 1980.

Changes in endorphins and 5-hydroxyindoleacetic acid (5-HIAA) in CSF as a result of treatment with a serotonin reuptake inhibitor, zimelidine, were studied in 20 chronic pain patients. Zimelidine produced significant pain relief and a significant reduction of the levels of endorphins and 5 HIAA in CSF, while no significant changes occurred during placebo treatment.

Results indicate that both the endorphin and the serotonin systems are involved in pain perception and that the systems are functionally related. 20 references. (Author abstract modified)

002202 Jusseume, Ph.; Martin, A.; Masson, J. M.; Voisin, Cl. Service de Psychiatrie B.C.H.R. Hôpital Bretonneau, 2, bld Tonnel, F-37033 Tours Cedex, France / **Trivastal 50 Retard in cerebral insufficiency of the elderly.** *Le trivastal 50 retard dans l'insuffisance cérébrale du sujet âgé.* *Revue de Geriatrie*. 4(7):377, 1979.

A psychotropic drug called Trivastal 50 Retard was tested on 11 hospitalized elderly mental patients and 10 outpatients, averaging 78 and 63 years respectively. It was found that the drug had positive effects on the patients acting as an easily tolerated psychotropic agent affecting subjective difficulties of sleep, anxiety, and depressive thymia. Its excellent tolerance makes it possible to increase the dosage from one pill a day to the usual dose given to outpatients, up to three pills a day in the case of the severe difficulties of hospitalized patients.

002203 Kaffman, M.; Sher, A.; Bar-Sinai, N. Kibbutz Child and Family Clinic, Seminar Hakibbutzim, Derech Haifa 147, Tel Aviv, Israel **MBD children - variability in developmental patterns of growth inhibitory effect of stimulants?** *Israel Annals of Psychiatry and Related Disciplines*. 17(1):58-66, 1979.

A clinical study was conducted with 50 kibbutz children with minimal brain dysfunction (MBD) in Israel to investigate a possible correlation between long-term amphetamine and Ritalin medication and suppression of physical growth. Experimental subjects received an average daily dose of 20mg of either amphetamine or Ritalin over a mean period of 3 years. Findings indicate that differences between the effects of the 2 drugs were nonsignificant; however, the height and/or weight of 9 of the 49 children fell below the first quartile after an average period of 2.8 years of medication. It is concluded that this inhibition of growth is not causally related to drug treatment because: 1) MBD children show a wide individual variability in their growth patterns, and 2) a bimodal height distribution existed prior to any medication, with concentrations in the lowest and highest quartiles. 17 references.

002204 Kahr, Frank M.; Riley, Mildred E. John Peter Smith Hospital, 1500 South Main Street, Fort Worth, TX 76104 **Long-term Diphenylhydantoin treatment of psychiatric patients.** *Hospital & Community Psychiatry*. 31(4):272-273, 1980.

A group of 12 severely impaired psychiatric patients who had been receiving diphenylhydantoin (DPH) for many years were studied to assess: 1) patients' drug compliance, 2) clinical status of the patients after long-term DPH use, and 3) significant side-effects of long-term DPH use. Half the patients whose serum DPH levels were measured were found to have levels far below the accepted therapeutic range and also below the level that would be predicted for their stated DPH dosage. It is reasonable to assume that these patients were not taking their medication as prescribed. That assumption raises the question of whether these patients, and other chronic psychiatric patients, are equally noncompliant with other regimens, such as antipsychotic medication. Only two patients were found to have minimal gingival hyperplasia, a common side-effect of long-term DPH use. It is suggested that patients, community workers, and foster parents be educated to the greatest extent possible about the indications for anticonvulsant treatment. 5 references.

002205 Kales, Anthony; Cadieux, Roger; Soldatos, Constantin R.; Tan, Tjiauw-Ling. Sleep Research and Treatment Center, Pennsylvania State University, Milton S. Hershey Medical Center, Hershey, PA 17033 **Successful treatment of narcolepsy**

with propranolol: a case report. *Archives of Neurology*. 36(10):650-651, 1979.

A case report of a patient with severe narcolepsy and cataplexy is presented. The patient had been treated with a high dosage of methylphenidate hydrochloride, but the drug was not effective. To relieve the patient's cardiac arrhythmia, which was assumed to be secondary to drug therapy, the methylphenidate therapy was withdrawn and propranolol hydrochloride therapy was started. When the dosage of propranolol was increased to a level consistent with maximum beta-adrenergic receptor blockade, the attacks were eliminated. 5 references. (Author abstract modified)

002206 Karson, Craig N. 3815 Van Ness St., NW, Washington, DC 20015 **Oculomotor signs in a psychiatric population: a preliminary report.** *American Journal of Psychiatry*. 136(8):1057-1060, 1979.

Oculomotor signs were evaluated in 172 psychiatric patients. Schizophrenic patients demonstrated a significantly higher incidence of staring, pursuit breaks, and lateral glances than did controls or other psychiatric patients. It is suggested that oculomotor signs may help to differentiate schizophrenia from affective and nonpsychotic disorders. Patients with tardive dyskinesia and patients treated with tricyclic antidepressants demonstrated a significant elevation in mean blink rate. It is suggested that elevated blink rates may be an early indicator of tardive dyskinesia. 13 references. (Author abstract)

002207 Kazamatsuri, Hajime; Hattori, Mineko. Dept. of Psychiatry, Teikyo University School of Medicine, Tokyo, Japan **Serum levels of phenytoin and phenobarbital in epileptic patients treated with mixture antiepileptic tablets, Comital-L or Hydantol-F.** *Folia Psychiatrica et Neurologica Japonica*. 33(3):319-322, 1979.

Serum levels of phenytoin and phenobarbital were determined by homogenous enzyme immunoassay in 59 epileptic patients treated chronically with common fixed dosage combination tablets of antiepileptic drugs (Comital-L or Hydantol-F), and the clinical rationale of prescribing mixture tablets showed low serum levels of phenytoin and high serum levels of phenobarbital, while patients treated with the usual daily dosage of Hydantol-F tablets showed adequate therapeutic serum levels of both phenytoin and phenobarbital. It is concluded that since the dosage of each anticonvulsant drug used concurrently should be established individually, the use of such fixed dosage mixture tablet of antiepileptic drugs in daily clinical practice should be reconsidered. (Author abstract modified)

002208 Keinänen-Kiukaanniemi, S.; Simila, S.; Luoma, P.; Kangas, L.; Saukkonen, A.-L. Department of Pediatrics, University of Oulu, Turku, Finland **Antipyretic effect and plasma concentrations of rectal acetaminophen and diazepam in children.** *Epilepsia*. 20(6):607-612, 1979.

The plasma levels of acetaminophen (paracetamol) and diazepam were measured in nine children by gas chromatography after administering these drugs simultaneously in separate suppositories. The antipyretic effects of oral and rectal acetaminophen/diazepam combinations were also studied and compared with that of oral or rectal acetaminophen alone. Diazepam at a dose of 0.2mg/kg did not increase the antipyretic action of acetaminophen. Acetaminophen and diazepam seemed to be well absorbed from the rectal suppositories. It is concluded that an acetaminophen/diazepam combination in separate suppositories may be suitable for the prevention of recurrent febrile convulsions in susceptible children, but its practical value and efficacy require evaluation in clinical experiments. 14 references. (Author abstract modified)

002209 Leonard, B. E. Pharmacology Dept., University College, Galway, Ireland **Pharmacological and biochemical aspects of hyperkinetic disorders.** *Neuropharmacology*. 18(12):923-929, 1979.

Pharmacological, neurological, and biochemical studies of hyperkinetic disorders are reviewed. Although neurological damage, genetic predisposition, viral infection, and lead toxicity may play a causative role in hyperkinetic behavior in some cases, there is insufficient evidence to implicate minimal brain damage as the primary cause of this behavior abnormality. The evidence implicating an abnormality in catecholamine or serotonin metabolism in the etiology of hyperkinetic disorder is largely circumstantial and based upon the supposed mode of action of stimulant drugs that are clinically effective in ameliorating symptoms of hyperkinetic disorders. 78 references.

002210 Lerer, Robert J.; Artner, Jeanne; Lerer, M. Pamela. 1277 Hicks Blvd., Fairfield, OH 45014 **Handwriting deficits in children with minimal brain dysfunction: effects of methylphenidate (Ritalin) and placebo.** *Journal of Learning Disabilities*. 12(7):450-455, 1979.

The effects of methylphenidate (Ritalin) on the handwriting difficulties of 50 hyperactive and learning disabled children were examined. The children received methylphenidate or placebo under double-blind conditions. Twenty-six (52%) showed improvement in overall handwriting following the administration of methylphenidate for 4 weeks. Many of their handwriting deficits, including letter reversals, improved or disappeared. Placebo had little appreciable effect. Direct observation of the students while writing suggested that advances in handwriting skills were related to improved visual/perceptual/motor function. It is concluded that methylphenidate has a direct positive effect on visual/perceptual/motor deficits often found in children with hyperactivity and learning disabilities. A number of practical applications for this finding are suggested. 13 references. (Author abstract)

002211 Linnoila, Markku; Simpson, Dale; Skinner, Travis. Box 3870, Duke University Medical Center, Durham, NC 27710 **Characteristics of therapeutic response to imipramine in cataplectic men.** *American Journal of Psychiatry*. 137(2):237-238, 1980.

Characteristics of patient response to imipramine in cases of narcolepsy and cataplexy were investigated. Data obtained from five male Ss indicates that: 1) the anticataplectic activity of imipramine has a rapid onset and the effect ceases rapidly on discontinuation; 2) a moderate tolerance to imipramine's anticataplectic activity occurred; 3) relatively low serum levels of imipramine and desipramine and the time course of therapeutic response in cataplectic patients are different from those of depressed patients, but similar to responses of hyperactive children; and 4) the mechanism of action in cataplexy and hyperactivity is different. 10 references.

002212 MacPhail, Ian; Ogilvie, W. Alasdair; Purvis, C. R. no address **Comparison of diazepam and flurazepam in the treatment of insomnia in general practice.** *Journal of International Medical Research*. 7(5):401-403, 1979.

Flurazepam was compared with diazepam in patients with a sleep disturbance who were treated by general practitioners. In a double-blind crossover study, flurazepam was shown to be significantly better (p less than .001) than diazepam in treating sleep disturbance. Flurazepam was found to be a more effective hypnotic in over 60% of the patients, whereas diazepam was effective in less than 19% of the patients. Fewer patients reported side-effects on flurazepam. 6 references. (Author abstract modified)

002213 Maltbie, Allan A.; Sullivan, John L.; Cavenar, Jesse O., Jr.; Hammett, Elliott B. Psychiatric Liaison Service, Veterans Administration Hospital, 508 Fulton St., Durham, NC 27705 **Haloperidol treatment of a sixty-year narcotic addiction: case report.** *Military Medicine*. 144(4):251-252, 1979.

The use of haloperidol for opiate withdrawal in an 82-year-old man who had been addicted for 60 years is reported. The man was withdrawn with a combination of methadone and haloperidol and then maintained on haloperidol alone. It is suggested that haloperidol could be a useful drug for withdrawal and maintenance in patients who are older and have a protracted period of addiction. 11 references.

002214 Manyam, N. V. B.; Hare, T. A.; Katz, L. Neurology Service, Veterans Administration Medical and Regional Office Center, Wilmington, DE 19805 **Effect of isoniazid on cerebrospinal fluid and plasma GABA levels in Huntington's disease.** *Life Sciences*. 26(16):1303-1308, 1980.

The effect of isoniazid on cerebrospinal fluid (CSF) and plasma GABA levels in patients with Huntington's disease was investigated. During a double-blind, placebo controlled trial, GABA was measured in CSF and plasma obtained prior to the start of the trial, at the end of the placebo period, and following treatment with isoniazid. Results show that the GABA concentrations in CSF tripled following treatment with isoniazid although no significant change occurred in plasma GABA levels. This finding in humans indirectly confirms reports of a similar increase of brain GABA content in experimental animals following isoniazid treatment and provides additional evidence that CSF GABA measurements reflect brain GABA activity. 37 references. (Author abstract modified)

002215 Matussek, N.; Ackenheil, M.; Hippus, H.; Muller, F.; Schroder, H.-Th.; Schultes, H.; Wasilewski, B. Psychiatric Hospital, University of Munich, Nussbaumstr. 7, D-8000 Munich 2, West Germany **Effect clonidine on growth hormone release in psychiatric patients and controls.** *Psychiatry Research*. 2(1):25-36, 1980.

The stimulation of human growth hormone (HGH) release by clonidine was studied as a test of postsynaptic alpha receptor sensitivity of psychiatric patients. Results reveal that endogenous depressives showed a significantly reduced HGH response to clonidine as compared to normal controls, neurotic/reactive depressives, and schizophrenics. However, no differences were found between the endogenous depressives and a group of schizoaffective patients. HGH response to clonidine was not correlated with plasma levels of noradrenaline, serum cortisol, free fatty acids, or blood glucose. Within the group of normal controls, a reduced HGH response was found in most postmenopausal women and in some regular users of alcohol. Results suggest that patients with endogenous depression are characterized by a subsensitivity of postsynaptic alpha receptors or of structures related to them. The clonidine test shows promise as an indicator of vulnerability to endogenous depression. 37 references. (Author abstract modified)

002216 Mehregan, Ursula; Krause, Klaus-Henning; Prager, Pedro. Krause: Neurologische Universitätsklinik, Vossstr.2, D-6900 Heidelberg, Germany **The frequency of adult anticonvulsant osteomalacia in relation to duration of therapy and dosage of anticonvulsants.** *Zur Häufigkeit der Osteopathia antiepileptica beim Erwachsenen in Abhängigkeit von Behandlungsdauer und Medikamentendosis.* *Archiv für Psychiatrie und Nervenkrankheiten*. 226(4):299-310, 1979.

The frequency of adult anticonvulsant osteomalacia in relation to duration of therapy and dosage of anticonvulsants was examined. Of 837 epileptics over 16 years of age treated with mono-

or combined hydantoin therapy, 20.3% showed radiographic signs of anticonvulsant osteomalacia. With the exception of the patients with severe disturbances of the skeletal system, no positive correlation was found with duration of therapy. The rate of osteomalacia correlated with the total dose of hydantoin, phenobarbital, or primidone. The rate of osteomalacia was the highest in the patients aged under 20 years and over 50 years. Males showed a relatively higher rate of osteomalacia than females; however, they were treated with a higher dose per year. It is concluded that early routine radiologic and chemical control especially of the epileptic patients with high risk of osteomalacia should be routinely performed in the future. 33 references. (Journal abstract modified)

002217 Meistrup-Larsen, Karen-Inger; Hermann, Stig; Permin, Henrik. Hermann: Hospital for Children in Vangede, 40 Sognevej, DK-2820 Gentofte, Denmark **Chronic diphenyl hydantoin encephalopathy in mentally retarded children and adolescents with severe epilepsy.** *Acta Neurologica Scandinavica*. 60(1):50-55, 1979.

Chronic diphenyl hydantoin (DPH) encephalopathy was studied in 21 mentally retarded epileptics with increasing psychomotor deterioration, choreiform hyperkinesia, deposits of immunoglobulins in the skin, and changes in serum immunoglobulins. Three months after withdrawal of DPH the condition proved partially reversible, from the clinical as well as laboratory point of view. Eleven patients were followed for 1 year after discontinuation of DPH and the findings were largely unchanged from the 3 month followup examination. Before the drug was withdrawn, seven patients exhibited deposits of immunoglobulins at the dermo epidermal junction and in vessel walls. At the end of 1 year such deposits were found in only three patients, all of whom were on another antiepileptic drug. 11 references. (Author abstract modified)

002218 Mendelson, Wallace B.; Caine, Eric D.; Goyer, Peter; Ebert, Michael; Gillin, J. Christian. Caine: University of Rochester Medical Center, 300 Crittenden Blvd., Rochester, NY 14642 **Sleep in Gilles de la Tourette syndrome.** *Biological Psychiatry*. 15(2):339-343, 1980.

The sleep of six Gilles de la Tourette syndrome patients was compared with that of nine normal volunteers. The untreated Tourette patients had 30% less delta sleep. When the patients were treated with haloperidol, their sleep values were indistinguishable from those of volunteers. There was little evidence of sedation except for decreased movement time in the treated patients compared to the volunteers. It is concluded that the response of abnormality of sleep to haloperidol, an agent for suppressing motor and vocal tics, may have implications regarding the basic neurophysiology of this disorder. 8 references. (Author abstract modified)

002219 Minde, Klaus K. Dept. of Psychiatry, University of Toronto, Toronto, Ontario, Canada **Psychopharmacologic treatment of hyperactive children.** Some thoughts on the social ecology of present day psychopharmacology. *Canadian Journal of Psychiatry*. 25(3):201-212, 1980.

Questions frequently encountered in the diagnosis and treatment of hyperactive children are discussed. An attempt is made to order these questions within an ecological frame of reference using Propger and Eccles' recent book model. Focus is on psychopharmacological treatment, such as methylphenidate, and cognitive and behavioral symptoms occurring in hyperactive children, as well as on the social relationships among children receiving drug treatment. The possible impact that psychostimulant treatment and the glamorization of drug taking behavior

may have on the structure of society at large is also examined. 24 references. (Author abstract modified)

002220 Mohs, Richard C.; Davis, Kenneth L.; Tinkenberg, Jared R.; Hollister, Leo E.; Yesavage, Jerome A.; Kopell, Bert S. Palo Alto Veterans Administration Hospital, Palo Alto, CA 94304 **Choline chloride treatment of memory deficits in the elderly.** *American Journal of Psychiatry*. 136(10):1275-1277, 1979.

The effect of choline chloride on memory deficits in the elderly was investigated. Eight elderly patients with mild memory impairment were given choline chloride, a drug that increases brain acetylcholine concentrations. After 16g/day of choline for 7 days, average memory performance was not different from performance during precholine and postcholine placebo treatment, although the patient with the poorest baseline performance improved considerably on choline. Overall, choline chloride did not affect performance of healthy elderly people on tasks involving storage and retrieval of information in memory. 20 references. (Author abstract modified)

002221 Monaco, Francesco; Mutani, Roberto; Mastropaolo, Camillo; Tondi, Massimo. Neurological Clinic, University of Sassari, Sassari, Italy **Tears as the best practical indicator of the unbound fraction of an anticonvulsant drug.** *Epilepsia*. 20(6):705-710, 1979.

Phenobarbital and carbamazepine concentrations were determined by the EMIT technique in tears, saliva, cerebrospinal fluid (CSF), and plasma of patients with epilepsy. Closer correlation was shown between tear/plasma and tear/CSF ratios than between saliva/plasma and saliva/CSF ratios for the two agents. The phenobarbital CSF/serum ratio was in good agreement with data in the literature, and the higher ratio found for carbamazepine may be caused by an EMIT assay cross-reaction for the free fraction of carbamazepine-10,11-epoxide. It is concluded that tears represent the best practical indicator of the unbound fraction of an anticonvulsant drug, and the noninvasiveness of the method makes it specifically useful in pediatric neurology. 16 references. (Author abstract)

002222 Munari, Claudio; Casaroli, Dionigio; Matteuzzi, Giorgio; Pacifico, Luigi. Unite de Recherches sur l'Epilepsie (U. 97), Centre Paul Broca de l'INSERM, F-75014 Paris, France **The use of Althesin in drug-resistant status epilepticus.** *Epilepsia*. 20(5):475-483, 1979.

The use of Althesin to treat 11 patients in status epilepticus resistant to the standard drugs is reported. The administration of Althesin by slow intravenous injection was ineffective in two of the three patients thus treated; the doses used (2 to 10ml) were probably too small. Only one administration of a 10% solution of Althesin in 10% fructose by intravenous drip stopped status epilepticus in seven of the nine patients thus treated. In this group, the doses used varied from 25 to 50ml. It is concluded that despite the very small number of cases, the definitive arrest of status epilepticus obtained in 8 of 11 cases first treated with other drugs is encouraging. 16 references. (Author abstract modified)

002223 Neborsky, Robert; Janowsky, David; Munson, Ethan; Hornbeck, Cecil; Depry, Dennis. Department of Psychiatry, University of California at San Diego, School of Medicine, La Jolla, CA 92139 **Behavioral prediction of response to haloperidol following a test dose strategy.** (Unpublished paper). Research Report, NIMH Grant 1P50-MH-30914, 1979. 14 p.

Twenty acutely-psychotic male patients were randomly divided into two groups and treated with rapid neuroleptization with high (10mg/dose) and low (2mg/dose) haloperidol to test the behavioral prediction of response. The test dose hypothesis was

supported by the finding that symptomatic improvement at 1 hour, after the first several hours, and after 24 hours significantly predicted improvement at the end of 7 days of haloperidol administration. Additionally, early change in the independent Brief Psychiatric Ratings Scale subscales of thinking disorders, excitement, and hostility suspiciousness proved to be significant predictors of ultimate improvement. Serum levels of haloperidol did not correlate significantly with improvement. 29 references. (Author abstract modified)

002224 Neborsky, Robert; Janowsky, David; Munson, Ethan; Depry, Dennis. Department of Psychiatry, University of California at San Diego, School of Medicine, La Jolla, CA 92139 **The rapid treatment of acute psychotic symptoms with high and low dose haloperidol: behavioral considerations.** (Unpublished paper). Research Report, NIMH Grant MH-30914, 1979. 26p.

Twenty acutely psychotic male psychiatric inpatients were divided into two groups and treated with high (10mg/dose) and low (2mg/dose) dose haloperidol with a rapid neuroleptization technique, followed by a 6 day maintenance phase. Both groups of patients improved overall at 1 hour, 1 day, and 7 days after start of treatment, and neither group differed as to degree or rapidity of symptom alleviation. Psychotic symptom alleviation at 1 hour and 1 day after start of treatment significantly predicted improvement at the end of the study. 29 references. (Author abstract)

002225 Nishihara, Kazuyo; Kohda, Yukinao; Saitoh, Yukiya; Honda, Yutaka. Hospital Pharmacy, Faculty of Medicine, University of Tokyo, Tokyo, Japan **Interaction between plasma phenytoin and phenobarbital concentrations in epileptic patients.** *Folia Psychiatrica et Neurologica Japonica*. 33(3):315-317, 1979.

The interaction between phenytoin (PHT) and phenobarbital (PB) in epileptic patients was studied by simultaneous determination of plasma concentrations in 158 epileptic outpatients. Most of the patients suffered bilateral generalized convulsions, and were maintained at steady state concentrations of PHT and/or PB. Results indicate that PB either accelerates the metabolism of PHT in the liver or inhibits the absorption of PHT from the gastrointestinal tract. Results also suggest that either metabolism of PB in the liver or excretion of PB from the kidney is inhibited by PHT. The use of a combination drug containing both PHT and PB is not recommended due to the unpredictability of the drug interaction. 6 references.

002226 no author. no address **Bromocriptine (therapeutics.** *Current Therapeutics*. 20(10):27-28, 30-32, 1979.

The use of bromocriptine (2-bromo-alpha-ergocryptine), a lysergic acid derivative with unique effects of dopamine receptors in the pituitary and central nervous system, on peripheral activity, is described. The major use of the drug is in the suppression of prolactin in states where this hormone is elevated, irrespective of the cause. In treating parkinsonism, bromocriptine has an overall effect similar to that of levodopa either alone or with genserazide when optimum doses are used. Individual patients may respond differently. The major dose limiting side-effects in parkinson patients are neuropsychiatric disturbances which occur frequently, as well as occasional vascular toxicity.

002227 no author. No address **Epilepsy after head trauma and fitness to drive.** *Lancet*. no. 8165:401-402, 1980.

The risk of epilepsy following head injury or intracranial surgery is discussed with reference to fitness to drive and treatment. The degree of risk of epilepsy after head injury has been found by Jennett (1975) to vary between 2% and 60% depending on the clinical features known within a week of injury. Figures from this study are available as a basis of advising patients

about driving. In addition, more than half of those patients who develop epilepsy following head injury do so within a year, and subsequent risk of traumatic epilepsy diminishes as the seizure free interval since injury increases. Statistics of epilepsy risk following intracranial surgery are less comprehensive than those for head injury and more extensive data is required before accurate risk estimates can be made. In addition, a number of studies have shown that treatment with phenytoin or sodium valproate is effective in reducing the incidence of postoperative epilepsy. It seems reasonable to advise a temporary embargo on driving for head trauma patients with an appreciable risk of epilepsy (say about 20%). Recent work with anticonvulsants may in part help resolve the dilemma for doctors who must advise on driving following head trauma. 16 references.

002228 North, J. Brian; Hanieh, Ahmad; Challen, Robert G.; Penhall, Robert K.; Hann, Christopher S.; Frewin, Derek B. Dept. of Neurosurgery, Royal Adelaide Hospital, Adelaide, South Australia **Postoperative epilepsy: a double-blind trial of phenytoin after craniotomy.** *Lancet*. No. 8165:384-386, 1980.

A double-blind trial of phenytoin in the prevention of postoperative epilepsy was conducted in 203 craniotomy patients. Results indicated that of 101 patients treated with phenytoin, eight (7.9%) evidenced epilepsy; while of 102 receiving placebo, epilepsy occurred in 17 (16.7%). Therapeutic drug levels were associated with a significant reduction in the frequency of epilepsy. Three quarters of the seizures occurred within a month of cranial surgery. Results suggest that routine prophylaxis is indicated in patients with meningioma, aneurysm, and head injury with or without intracranial clots as high rates of postoperative seizure have been observed in such patients. 8 references. (Author abstract modified)

002229 Nutt, John G.; Kupferberg, Harvey J. Experimental Therapeutics Branch, National Institute of Neurological and Communicative Disorders and Stroke, NIH, Bethesda, MD 20014 **Linear relationship between plasma concentration and dosage of sodium valproate.** *Epilepsia*. 20(6):589-592, 1979.

Plasma valproate concentration was studied in seven hospitalized nonepileptic patients who received sodium valproate at daily doses up to 60mg/kg. A linear relationship between dose and plasma concentration of valproate was found in each patient, although the slopes of the regression lines (reflecting clearance rates) varied twofold. This suggests that if the valproate plasma concentrations at two different doses are known and the clearance of valproate is not altered by concomitant administration of other drugs, it should be possible to predict the plasma valproate concentration that will result from further dose increments. 9 references. (Author abstract)

002230 Parkes, J. D.; Schachter, M. University Dept. of Neurology, King's College Hospital and Institute of Psychiatry, London SE5, England **Clomipramine and clonazepam in cataplexy.** *Lancet*. No. 8151:1085-1086, 1979.

The treatment of 75 cataplexy patients with clomipramine for 4 to 7 years and the treatment of 14 cataplexy patients with clonazepam for 2 to 36 months are described. Good to excellent responses to the drugs are reported, with immediate increase in the severity of cataplexy symptoms following drug withdrawal. It is noted that if these findings are confirmed, clonazepam may replace clomipramine as the drug of first choice in the treatment of cataplexy and sleep paralysis. 3 references.

002231 Pena-Ramos, Abelardo; Hornberger, Robert. Dept. of Psychiatry (116A), VA Hospital, 13000 North 30th Street, Tampa, FL 33612 **MMPI and drug treatment in alcohol withdrawal.** *Journal of Clinical Psychiatry*. 50(8):361-364, 1979.

In an examination of the personality structures of alcoholic patients and the efficacy of drug treatment, 34 inpatients in a mild phase of alcohol withdrawal, exhibiting anxious and depressive symptoms, were administered an MMPI before and immediately after a 4 week drug treatment period. A double-blind design was used; 17 patients were treated with chlorthalidone and 17 with thioridazine. The pretreatment MMPI profile was typical of alcoholic patients; namely peaks on scales 4 and 2. After the fourth week, the MMPI indicated that thioridazine was significantly more effective than chlorthalidone. Decreases in 7 of the 10 clinical scales averaged 7.29 T-score points, whereas only scale 6 was significantly decreased for the patients treated with chlorthalidone. 9 references. (Author abstract)

002232 Pollack, Michael A.; Zion, Thomas E.; Kellaway, Peter. Section of Neurophysiology, Dept. of Neurology, Baylor College of Medicine, Houston, TX 77025 **Long-term prognosis of patients with infantile spasms following ACTH therapy.** *Epilepsia*. 20(3):255-260, 1979.

The long-term benefits of initially successful corticotropin (ACTH) therapy in patients treated between 1961 and 1974 were examined. Eighteen affected infants showed a favorable early response consisting of cessation of seizures for at least 3 weeks during ACTH therapy and concurrent disappearance of the hypsarrhythmic EEG pattern. Age at last followup ranged from 15 months to 16 years. Infantile spasms recurred in 7 patients, and 8 patients subsequently had other seizure types. All epileptiform activity disappeared from the EEGs of 8 patients during ACTH therapy, but in 4 of these cases epileptiform activity was present in later tracings. In the remaining 10 patients the hypsarrhythmic pattern disappeared in association with ACTH therapy, but the EEG remained epileptiform. Later EEGs were free of discharges in the early followup period. Four patients were seizure free and without intellectual impairment when last evaluated. 10 references. (Author abstract modified)

002233 Porte, M.; Juttner, G.; Michelangeli, J.; Krebs, B. P.; Lavagna, J.; Capdeville, C.; Darcourt, G. Service de Psychiatrie et de Psychologie medicale, Hopital Pasteur, F-06031 Nice, Cedex, France **Delayed action Synacthene in states of mental confusion in elderly patients.** *Le Synacthene-Retard dans les confusions mentales des sujets ages.* *Annales Medico-Psychologiques*. 137(5):481-490, 1979.

The effects of tetracosactide, sold by the Ciba Laboratories under the commercial name of Synacthene-Retard (delayed action Synacthene), were studied. The drug was administered intramuscularly to 15 subjects over 65 years of age in doses of 1mg per day; a placebo was given to 13 subjects. All these patients suffered from organic disorders of the brain, with bonubilation or mental confusion. It was found that the adrenal cortex of the patient responded very well to the stimulation by Synacthene. The product improved the symptoms of confusion. Its tolerance was good. The drug was particularly effective when mental confusion was due to a cerebral vascular cause. The effectiveness was not proportionate to the rate of increase of cortisolemia. A discussion follows the text of the article. 3 references. (Author abstract modified)

002234 Redenbaugh, J. E.; Sato, S.; Penry, J. K.; Dreifuss, F. E.; Kupferberg, H. J. Sato: Federal Building, Room 114, NIH, Bethesda, MD 20205 **Sodium valproate: pharmacokinetics and effectiveness in treating intractable seizures.** *Neurology*. 30(1):1-6, 1980.

The pharmacokinetics and effectiveness in treating intractable seizures of sodium valproate were assessed in a pilot study of 20

patients (10 adults and 10 children). The drug was absorbed and excreted rapidly; the mean half-life was 916 hours. Drowsiness and gastrointestinal symptoms were the most common side-effects, but they were usually minor and transient. An increase in some plasma phenobarbital levels and a decrease in some plasma phenytoin levels were attributed to drug interaction. Control of absence attacks was assessed by 12 hour telemetered electroencephalograms. Sodium valproate was found most efficacious in generalized seizure disorders, particularly absence seizures. 17 references. (Author abstract modified)

002235 Reimherr, Frederick W.; Wood, David R.; Wender, Paul H. Wender: Dept. of Psychiatry, University of Utah College of Medicine, Salt Lake City, UT 84132 **An open clinical trial of L-dopa and carbidopa in adults with minimal brain dysfunction.** *American Journal of Psychiatry*. 137(1):73-75, 1980.

To test the hypothesis that one form of minimal brain dysfunction (MBD) is a consequence of reduced activity of dopaminergic systems in the brain, three adults with presumptive MBD were given L-dopa plus carbidopa. Although overall this combination was less effective than stimulant medication, all the patients showed an initial response, and in one patient L-dopa seemed to potentiate the effect of methylphenidate. It is concluded that various dopamine agonists have different effects and that the possible potentiation effect is consistent with a dopaminergic hypothesis. 10 references. (Author abstract modified)

002236 Reisine, T. D.; Azari, J.; Johnson, P. C.; Barbeau, A.; Huxtable, R.; Yamamura, H. I. Barbeau: Clinical Research Institute of Montreal, 110 Pine Ave. West, Montreal, Quebec, Canada H2W 1R7 **Brain neurotransmitter receptors in Friedreich's ataxia.** *Canadian Journal of Neurological Sciences*. 6(2):259-262, 1979.

The binding of 3H-quinuclidinyl benzilate, a muscarinic cholinergic antagonist, of 3H-dihydroalprenolol, a beta-adrenergic antagonist, and of 3H-flunitrazepam, a ligand which labels benzodiazepine receptors, was examined in several regions of control and Friedreich's ataxia (FA) brains. 3H-Quinuclidinyl benzilate binding appeared to increase in the inferior olivary nucleus, anterior and posterior cerebellar vermi but was unaltered in the dentate nucleus and cerebellar hemisphere of FA brain. The binding of 3H-dihydroalprenolol seemed to increase in the inferior olivary nucleus yet was not different from controls in the dentate nucleus, cerebellar hemisphere, anterior and posterior cerebellar vermi of FA brains. 3H-Flunitrazepam binding was slightly lowered in the inferior olivary and dentate nuclei but was unchanged in the other FA brain regions examined. 10 references. (Author abstract modified)

002237 Renvoize, E. B.; Jerram, Timothy. University of Leeds, Leeds LS2 9ET, England **Choline in Alzheimer's disease.** *New England Journal of Medicine*. 301(6):330, 1979.

In order to determine the effects of choline in Alzheimer's senile or presenile dementia, a 2 month double-blind study compared choline chloride in a dose of 15g per day with a placebo mixture among 18 female patients, 57 to 84 years old. The patients were assessed before, during, and after treatment with a dementia scale, the Crichton Behavior Rating Scale, and a scale that measures the ability to communicate. The results showed no important differences between patients who received choline and those who received placebo. 10 references.

002238 Rinne, U. K.; Molsa, P. Dept. of Neurology, University of Turku, SF-20520 Turku 52, Finland **Levodopa with benserazide or carbidopa in Parkinson disease.** *Neurology*. 29(12):1584-1589, 1979.

Plasma levodopa and therapeutic response to treatment with levodopa in combination with benserazide or carbidopa were studied in 49 patients with idiopathic Parkinson disease not previously treated with levodopa, in a blind randomized crossover trial. Treatment periods were 12 weeks, and similar dosage schedules were used, with doses that induced equal levels of plasma levodopa in both combinations. In pretrial studies, 200mg levodopa and 50mg benserazide was equal to 250 mg levodopa combined with 25mg carbidopa. Equal plasma levodopa responses to both combinations were also found during the trial. There was no significant difference between groups in beneficial effects on parkinsonian disability and individual symptoms or in the frequency of involuntary movements. However, nausea and vomiting occurred significantly more often for the levodopa/carbidopa treatment. This difference was probably due to inadequate inhibition of peripheral decarboxylase inhibitor by the 1:10 ratio of carbidopa to levodopa. 13 references. (Author abstract)

002239 Robbins, T. W.; Sahakian, B. J. Psychological Laboratory, Dept. of Experimental Psychology, Downing St., Cambridge CB2 3EB, England **Hyperactive children from the standpoint of behavioural pharmacology.** *Neuropharmacology*. 18(12):931-950, 1979.

The use of psychomotor stimulant drugs in treating childhood hyperkinesis is discussed in relation to the hypothesized paradoxical drug effect. Studies in normal children and adults as well as hyperkinetic children suggest that the so called paradoxical drug effect observed in hyperkinetic children reflect abnormalities in these children's behavior in the absence of the drug. The rate reducing effects of the drugs such as amphetamine and methylphenidate may arise as a consequence of the high rates of control responding in the hyperactive child. Similarly, the effects of stimulants on attention may be related to overfocusing or lack of cognitive flexibility in hyperactive children. Rate dependency, attention and stereotypy, and subjective and social effects of drugs are discussed in relation to clinical practice and animal models of the hyperkinetic syndrome. 98 references. (Author abstract modified)

002240 Robichaud, Colleen; Strickler, Daniel; Bigelow, George; Liebson, Ira. Bigelow: Dept. of Psychiatry, Baltimore City Hospitals, Baltimore, MD 21224 **Disulfiram maintenance employee alcoholism treatment: a three phase evaluation.** *Behaviour Research and Therapy*. 17(6):618-621, 1979.

Absenteeism rates of industrial employees referred by their employers for alcoholism treatment were evaluated during three phases: pretreatment, treatment, and posttreatment. Treatment consisted of disulfiram maintenance, routine supervised ingestion of disulfiram, without scheduled counseling. The median percent of scheduled work days absent for each phase was: pretreatment, 98%; treatment, 1.7%; posttreatment, 6.7%. Absenteeism during the treatment phase was significantly less than during pretreatment and posttreatment, which did not differ significantly from one another. The five fold reduction in absenteeism is specifically related to treatment delivery, and appears superior to the two fold reduction reported for traditional employee alcoholism treatment via counseling. 9 references. (Author abstract modified)

002241 Roth, Thomas; Tietz, Elizabeth I.; Kramer, Milton; Kaffeman, Mark. Sleep Disorders and Research Center, Henry Ford Hospital, Detroit, MI **The effect of a single dose of quazepam (Sch-16134) on the sleep of chronic insomniacs.** *Journal of International Medical Research*. 7(6):583-587, 1979.

The efficacy of 25mg of quazepam (Sch-16134), a new benzodiazepine hypnotic, in a population of chronic insomniacs was

evaluated. A single dose administered for one night was efficacious when measured both objectively by polysomnographic recording and subjectively by questionnaire, and no reported side-effects were noted. Changes in the objective measures paralleled the direction of changes in the subjective measures. Sleep efficiency and sleep maintenance were improved without EEG changes in Stages 2, 3, 4, and REM. The effects of chronic administration at different doses should be further investigated. 3 references. (Author abstract modified)

002242 Salzman, Carl; van der Kolk, Bessel. Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Psychotropic drug prescriptions for elderly patients in a general hospital.** *Journal of the American Geriatrics Society.* 28(1):18-22, 1980.

A survey of drug prescriptions written for all medical/surgical patients in a general hospital is described, and the psychotropic drug prescriptions for elderly patients are reviewed. Of 348 patients, 195 were over the age 60 years. In this elderly group, 62 were receiving psychoactive drugs. Flurazepam was the drug most commonly prescribed (in 63% of the patients). Diazepam was the most frequently prescribed nonhypnotic psychoactive drug (in 29%). Neuroleptic drugs and phenothiazine antiemetics (in 52%) were not prescribed for psychosis but for augmenting analgesia and sedation and for reducing nausea. The average daily doses were about 20% of those used to treat psychotic young adults. All antidepressants had been prescribed before admission. No MAO inhibitors were used, and doses of tricyclic antidepressants were half to one third lower than those used to treat younger depressed adults. Antidepressants, which pose a risk to the elderly patient, were overprescribed and underdosed. 20 references. (Author abstract modified)

002243 Sampson, Gwyneth A. Queenswood Unit, Middlewood Hospital, Sheffield S6 1TP, England **Premenstrual syndrome: a double-blind controlled trial of progesterone and placebo.** *British Journal of Psychiatry.* 135(September):209-215, 1979.

Patients with premenstrual syndrome recorded their symptoms daily using menstrual distress questionnaires in a double-blind controlled trial of progesterone and placebo treatments. Eight symptoms clusters (pain, concentration, behavioral change, autonomic reaction, water retention, negative affect, arousal, and symptoms reflecting a general tendency to complain) were developed, and Ss received progesterone and placebo treatments whose efficacy was determined by daily distress questionnaires and retrospective self-assessment. No significant differences between the two treatments were noted, and in most cases the placebo was nonsignificantly more effective. A secondary finding in progesterone treated patients included more positive feelings of affection, orderliness, excitement, feeling of well-being, and bursts of energy. 13 references. (Author abstract modified)

002244 Schiff, Isaac; Regestein, Quentin; Tulchinsky, Dan; Ryan, Kenneth J. Boston Hospital for Women, 221 Longwood Avenue, Boston, MA 02115 **Effects of estrogens on sleep and psychological state of hypogonadal women.** *Journal of the American Medical Association.* 242(22):2405-2407, 1979.

The effects of placebo and conjugated estrogens on gonadotropin levels, symptoms, sleep patterns, and psychological state were compared in 16 hypogonadal women. After 1 month, serum concentrations of follicle stimulating hormone fell 31%, and levels of luteinizing hormone, 19%. The number of vasomotor flushes also decreased. The administration of estrogens was also associated with a shorter mean sleep latency, a longer period of rapid eye movement sleep, and a positive correlation between psychological intactness, and latency to sleep onset.

Psychological testing, including the Clyde Mood Scale, and the Gottschalk-Gleser Test indicated that estrogens caused this group to be less outwardly aggressive but more inwardly hostile. 14 references. (Author abstract)

002245 Schneider-Helmert, D.; Schenker, J.; Gnirss, F. Research Dept., Psychiatric Clinic, CH-5200 Königsfelden, Switzerland **Deficient blood pressure regulation in a case of hypersomnia with sleep drunkenness.** *Electroencephalography and Clinical Neurophysiology.* 48(2):230-232, 1980.

Polygraphic sleep recordings and direct blood pressure (BP) measurements were obtained in a 43-year-old man suffering from hypersomnia with sleep drunkenness (HSD). The patient had been successfully treated for depression and psychosomatic symptoms with antidepressants and psychotherapy, but the HSD persisted. The sleep study showed that BP activation was absent during arousal from sleep and after morning awakening, indicating that cardiovascular responses to activating stimuli were too weak. The sleep drunkenness and daytime sleepiness were alleviated by etilefrine, which sustains BP. 5 references.

002246 Sherard, Earl S., Jr.; Steiman, Gerald S.; Couri, Daniel. 700 Children's Drive, Columbus, OH 43205 **Treatment of childhood epilepsy with valproic acid: results of the first 100 patients in a 6-month trial.** *Neurology.* 30(1):31-35, 1980.

The evaluation of valproic acid (VPA) in the treatment of 100 cases of childhood epilepsy during a 6 month period is described. Of the 100 patients, 38 had partial seizures and 62 suffered from generalized epilepsy. Sixty-one patients experienced more than a 75% decrease in seizures. The improvement in generalized epilepsy paralleled adults VPA studies, but partial epilepsy improved more than expected, even though acceptable seizure control was often achieved only after 6 months of VPA therapy. The most significant side-effect was gastrointestinal distress, which was alleviated by dietary changes. Limited experience suggests that enteric coated capsules eliminated gastrointestinal symptoms. Hematologic, hepatic, and behavioral sequelae were minimal. 18 references. (Author abstract modified)

002247 Sillanpaa, Matti; Pynnonen, Seppo; Laippala, Pekka; Sako, Erkki. Dept. of Pediatrics, University of Turku, Turku 52, Finland **Carbamazepine in the treatment of partial epileptic seizures in infants and young children: a preliminary study.** *Epilepsia.* 20(5):563-569, 1979.

A study of 19 pediatric patients 3 months to 14 years of age successively hospitalized for partial epileptic seizures in which carbamazepine (CBZ) was the first and only drug in 18 patients and the subsequent but only drug in 1 is reported. Blood concentrations of CBZ and carbamazepine-10,11-epoxide (CBZ-E) were determined by gas-liquid chromatography. During the mean followup period of 12 months the frequency of seizures was reduced by 75% to 100% in 11 patients and 50% to 74% in 2 more patients. Daily dosage, effect of CBZ concentrations on clinical effects, and relations of treatment to a patient's age are also discussed. 12 references. (Author abstract modified)

002248 Spriet, Alain; Beiler, Daniel; Dechorgnat, Jean; Simon, Pierre. Dept. Medical, Laboratoires Hoechst, 3, avenue du General-de Gaulle, F-92800 Puteaux, France **Adherence of elderly patients to treatment with pentoxifylline.** *Clinical Pharmacology and Therapeutics* 27(1):1-8, 1980.

A study of adherence to treatment was conducted by 179 general practitioners in elderly outpatients with geriatric cerebral symptomatology treated with pentoxifylline. Compliance was assessed by pill count after 1 month of treatment. Leftover drug was returned by 83.1% of the patients, but compliance was considered good in 62%. Compliance was not affected by pack-

aging or by memory aid stickers. Compliance was not related to age or sex, but was related to memory score. There was a correlation between compliance and clinical improvement and a significant inverse correlation between compliance and the frequency of side-effects. 29 references. (Author abstract modified)

002249 Steiner, Meir; Haskett, Roger F.; Osmun, Judith N.; Carroll, Bernard J. Dept. of Psychiatry, Mental Health Research Institute, University of Michigan Medical Center, Ann Arbor, MI 48109 **Treatment of premenstrual tension with lithium carbonate: a pilot study.** *Acta Psychiatrica Scandinavica*. 61(2):96-102, 1980.

To investigate the effect of lithium on premenstrual tension, 15 women selected for severe premenstrual tension syndrome (PMTS) were given lithium carbonate (600 to 900mg/day) continuously for three menstrual cycles. Lithium did not affect physical premenstrual symptoms and was ineffective in most women against behavioral premenstrual symptoms. Despite the low dosage most women also experienced significant drug related side-effects. Although a statistically significant improvement was recorded by several symptom rating instruments, this benefit was of no practical clinical value. The three women who responded best to lithium, and who requested continued treatment beyond 3 months, met diagnostic criteria for subsyndromal affective (cyclothymic) disorder. Lithium is not recommended for the average woman with PMTS. 16 references. (Author abstract modified)

002250 Strobe, Barbara E.; Hollenbeck, Albert R.; Susman, Elizabeth J.; Nannis, Ellen D. Laboratory of Developmental Psychology, NIMH, Bethesda, MD 20205 **Behavioral studies of seriously ill children. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 3 p.

Four children, 18 to 48 months old, who were confined to a Laminar Air Flow (LAF) room during their chemotherapy treatment, were studied to determine whether children undergo changes in behavior in this hospital setting. The behavior of the children was videotaped for 10 minutes every morning and afternoon, 5 days per week, for up to 7 weeks of treatment. The data confirm previous findings which suggest that the effects of isolating environments for young children have a depressive behavioral effect. Furthermore, the increasing passivity and nonsocial behavior appears to be independent of even severe medical interventions.

002251 Strobe, Barbara E.; Susman, Elizabeth J.; Hollenbeck, Albert R.; Nannis, Ellen D. Laboratory of Developmental Psychology, NIMH, Bethesda, MD 20205 **The behavior of young children in protected environments during chemotherapy. (Unpublished paper).** Bethesda, MD, NIMH, 1979. 2 p.

Children subjected to long periods of treatment in isolation environments were studied in an exploration of changes in behavior hypothesized to coincide with the starting and stopping of chemotherapy. Specifically, it was hypothesized that periods of chemotherapy would greatly reduce the children's social behavior, but that over time social behavior would return to baseline levels. Four children, 18 to 48 months old, were confined to semisolation as part of their treatment protocol. The behavior of the children was videotaped for 10 minutes every morning and afternoon, 5 days per week, for up to 7 weeks of treatment. Sleeping was found to be the critical behavior, and, thus, sleeping was used as a criterion for exploring subsequent behaviors of the children during baseline, chemotherapy, and recovery periods. The data confirm previous findings which suggest that the effects of isolating environments for young children have a depressive behavioral effect. Furthermore, the increasing passiv-

ity appears to be predictable and induced by periods of chemotherapy.

002252 Taylor, E. Institute of Psychiatry, University of London, De Crespigny Park, Denmark Hill, SE5 8AK, England **The use of drugs in hyperkinetic states: clinical issues.** *Neuropharmacology*. 18(12):951-958, 1979.

A review of the use of stimulant drugs in hyperactive children reveals large variation in clinical practice, due to confusion about the nature of the disorder, the action of the drugs, the prediction of drug action, and the severity of undesirable long-term side-effects. Hyperactivity appears to be a heterogeneous collection of symptoms with different aetiologies. The stimulant drugs do not reverse any specific pathology, but exert multiple effects on various aspects of behavior and cognition. It is recommended that stimulants such as methylphenidate and amphetamine be used with caution, when psychological means of treatment are not effective. The stimulant drugs do appear to be of value in treating some forms of impaired attention. 42 references. (Author abstract modified)

002253 Teravainen, Heikki; Calne, Donald B. Calne: National Institute of Neurological and Communicative Disorders & Stroke, NIH, Bldg. 10, Rm. 6D-20, Bethesda, MD 20205 **Developments in understanding the physiology and pharmacology of parkinsonism.** *Acta Neurologica Scandinavica*. 60(1):1-11, 1979.

Progress that is being made in elucidating physiological and pharmacological aspects of Parkinson's disease is reviewed. The main components involved in voluntary and involuntary movements in parkinsonism are diagrammed. Physiological analysis of Parkinsonism has elucidated certain aspects of the cardinal features of parkinsonism: rigidity, tremor, and the less obvious but most incapacitating deficits, akinesia and bradykinesia. The dramatic impact of levodopa therapy has been followed by the recognition of serious limitations to its long-term use, which provides a continuing stimulus for efforts to analyze the physiological and pharmacological properties of the basal ganglia and substantia nigra. There are reasonable grounds for the hope that this research will lead to significant developments in therapy. 40 references. (Author abstract modified)

002254 Thurston, Catherine M.; Sobol, Michael P.; Swanson, James; Kinsbourne, Marcel. Sobol: Dept. of Psychology, University of Guelph, Guelph, Ontario, Canada N1G 2W1 **Effects of methylphenidate (Ritalin) on selective attention in hyperactive children.** *Journal of Abnormal Child Psychology*. 7(4):471-481, 1979.

The effect of methylphenidate (Ritalin) on the selective attention of 54 hyperactive children designated as favorable or adverse responders to stimulant medication was investigated. Using a type II incidental learning paradigm, it was found that children in the drug condition recalled more central and less incidental stimuli than those children in the placebo condition. While no differential effect on recall were found for responder type, methylphenidate did affect the spontaneous overt labeling of central stimuli by the favorable responder group. Results are interpreted in terms of the role of methylphenidate in narrowing the focus of attention. Implications for the classification of hyperactives as favorable and adverse responders are also considered. 37 references. (Author abstract)

002255 Thurston, Linda P. Juniper Gardens Learning Center, Bureau of Child Research, University of Kansas, 1907 N. 3rd St., Kansas City, KS 66101 **Comparison of the effects of parent training and of Ritalin in treating hyperactive children.** *International Journal of Mental Health*. 8(1):121-128, 1979.

An investigation of the effects of training parents to use behavior modification procedures to reduce their children's hyperactive behavior is presented which compared these effects with those of a group on Ritalin therapy and a control group which received no treatment until after the study. Eighteen children, aged 6 to 9 years, labeled hyperactive, were divided into two treatment groups and a control group, approximately equal in age and sex. Actometer measures of hyperactivity, parent ratings of activity, and psychometric measures of impulsivity all showed decreases for both the Ritalin group and the parent training group. Parents' evaluations showed that those who participated in the parent training group were significantly more pleased with the treatment than were the parents whose children were given Ritalin. Because of the side-effects of the drugs, parental attitudes about drugs, possible long-term effects of drugs, and because the parent training procedure seems as effective, it is recommended as a viable alternative to the current practice of pharmacotherapy for hyperactivity. 13 references.

002256 Tonetto-Reis, Telmo; Soares-Maia-Filho, Manoel; Celso-Cechini, Pedro. Clinica Neurológica e Neurocirúrgica de Porto Alegre, Rua Mostardeiro 291, 90000 Porto Alegre RS, Brazil /Clinical evaluation of the therapeutic value of barhexacalone including the study of serum barbiturate levels./ Avaliacao clinica do valor terapeutico do barhexacalone incluindo determinacao de niveis plasmaticos do barbiturico. Arquivos de Neuro-Psiquiatria. 38(1):93-98, 1980.

Results of the use of barhexacalone (1-1-cyclohexyl-2-methylamino-propan) in association with phenylethylbarbiturate, as a single anticonvulsant drug in a clinical and therapeutic trial are reported. Seventy patients, 36 women and 34 men, 52 children and 18 adults, all of them with two or more epileptic grand-mal seizures at the beginning of treatment, were selected. In 53 patients, a complete 18 month followup observation was performed. In this group of patients, 96% of them were free of seizures during the followup period. In 20 patients, barbiturate plasma concentration was measured. For these patients, the effectiveness of the treatment was complete control of convulsive crises in 89% of patients. It is noted that measurement of plasma level of anticonvulsants is a useful and safe therapeutic guide in the treatment of epilepsies. 17 references. (Journal abstract modified)

002257 Versiani, Marcio; da Silva, J. A. R.; Mundim, F. D. Mayer-Gross Clinic, Rua Gonzaga Bastos 181 - ZC 11, Rio de Janeiro 20,000, Brazil Loxapine versus thioridazine in the treatment of organic psychosis. Journal of International Medical Research. 8(1):22-30, 1980.

Loxapine and thioridazine were compared over 13 weeks in two double-blind trials for effectiveness in treating chronic hospitalized psychotics with organic brain syndrome or mental retardation. The drugs were administered orally in with 10 to 150mg/day doses of loxapine and 150 to 750mg/day doses of thioridazine. Loxapine was generally superior in the first trial on the Brief Psychiatric Rating Scale, Nurses Observation Scale for Inpatient Evaluation, and Clinical Global Impression. This superiority was not confirmed in the second trial. The heterogeneity of diagnostic categories may explain this discrepancy. Extrapyramidal symptoms and sedative effects were common to both groups and were consistent with the pharmacologic profiles of the drugs. 8 references. (Author abstract modified)

002258 Villeneuve, A.; Cazejust, T.; Cote, M. Faculty of Medicine, Laval University, Quebec, PQ, Canada Estrogens in tardive dyskinesia in male psychiatric patients. Neuropsychobiology. 6(3):145-151, 1980.

The therapeutic effects of estrogens on tardive dyskinesia in male psychiatric patients were investigated. Conjugated estrogens (CE) were administered to 20 male chronic psychiatric patients (age range 29 to 63 years). All except one patient were receiving neuroleptic medication and eight Ss were receiving an antiparkinsonian agent. Patients were divided into four groups, all of whom received daily CE at different doses (1.25 or 2.50mcg) for a period of 6 weeks. A significant decrease in intensity or disappearance of one type of dyskinesia was observed in each group (four of five patients). No definite trend was noted in neuroleptic-induced Parkinsonism, or apparent change in the mental condition of the patients. The functioning of the extrapyramidal system is considered increasingly complex if this antidopaminergic action of estrogens is added. It has been hypothesized that, in addition to dopamine and acetylcholine, substances like GABA and enkephalin could also be involved in its regulation. The relationship between dopamine and estrogens is discussed in relation to the presence of estrogens in some areas of rat brain. It is hypothesized that the reported prompt and transitory rise in serum prolactin level after electroconvulsive therapy (ECT) may reflect a possible involvement of endorphins, at least in part, in the therapeutic effect of ECT. The possible influence of this form of treatment on extrapyramidal symptoms in relation with this is briefly discussed. 19 references. (Author abstract modified)

002259 Wagemaker, Herbert, Jr.; Lippmann, Steven; Bryant, David R. Dept. of Psychiatry, Louisville General Hospital, Louisville, KY 40212 Lithium response of a patient diagnosed as a paranoid schizophrenic. Psychiatric Opinion. 16(10):45-47, 1979.

A case history of a man diagnosed as paranoid schizophrenic who responded well to lithium therapy is reported. The question of how many patients diagnosed as schizophrenic fall in the classification of affective disorders and are lithium responders is raised. Trying lithium on patients who present with affective components such as depression, mania, or hostility is recommended. Conjoint use of lithium and neuroleptics is described. 4 references.

002260 Werry, John S.; Aman, Michael G.; Diamond, Eileen. Dept. of Psychiatry, School of Medicine, University of Auckland P.B., Auckland, New Zealand Imipramine and methylphenidate in hyperactive children. Journal of Child Psychology and Psychiatry and Allied Disciplines. 21(1):27-35, 1980.

The effects of imipramine and methylphenidate (Ritalin) on the behavior of hyperactive children were investigated with emphasis on physiological response, cognitive functioning, self-image, and dosage. There were positive effects on learning, motor performance, and social behavior, but self-esteem showed only minimal fluctuations. Certain physiological measures were adversely affected by the drugs. Few significant dose effects occurred, but, in general, the changes suggest that the lower dose results in less motor tremor and slightly superior clinical response. The effect of imipramine was similar to that of methylphenidate, suggesting a stimulant-like action. In contrast to other studies, imipramine was clinically more effective than methylphenidate in the short-term, but the side-effects were greater. 24 references. (Author abstract modified)

002261 Wilson, Allan. Dept. of Psychiatry, University of Manitoba, Winnipeg, Manitoba R3E 0W3, Canada Patient management in disulfiram implant therapy. Canadian Journal of Psychiatry. 24(6):537-541, 1979.

Data from 100 disulfiram implant, placebo, and no implant control patients are examined to illustrate the drug's effectiveness in alcoholic patient management. The observed superiority

of the disulfiram implant group over the placebo group provides evidence of pharmacological component to the procedure which operates independently of the disulfiram/ethanol reaction (DER). Inhibition of aldehyde dehydrogenase or inhibition of dopamine-beta-hydroxylase may be responsible for this effect. Since there is a low probability of DER following alcohol ingestion by a disulfiram implant patient, the approach to patient management should be changed to maximize effectiveness and guidelines for such procedures. 18 references.

002262 Witts, D. J.; Bowhay, A. A.; Garland, M.; McLean, A. E. M.; Exton-Smith, A. N. Department of Clinical Pharmacology, University College Hospital Medical School, London WC1, England **Studies of chlormethiazole in the elderly: pharmacokinetic aspects.** *Age and Ageing*. 8(4):271-284, 1979.

An analysis of the pharmacokinetic aspects of chlormethiazole use in the elderly considers physiological changes in old age, side-effects of hypnotics, plasma drug levels and hangover effect, and preliminary findings from a clinical trial of nitrazepam versus chlormethiazole in the elderly. Studies have shown conclusively that chlormethiazole is at least as effective or is superior to existing medication in the treatment of insomnia, confusional states, in the management of alcoholic and narcotic withdrawal, preeclamptic toxemia, and status epilepticus. In all studies where the clinical efficacy of chlormethiazole was similar to that of existing medication, chlormethiazole was preferred on the basis of ease of use and reduced incidence of side-effects. Little is known about the residual effects of hypnotics although both accumulation and hangover effects are commonly seen among the barbiturates and benzodiazepines. A computer prediction that those drugs with long half-lives will accumulate in the elderly and the original assumption that drug activity is related to the amount of drug in the body are supported by clinical evidence. Nitrazepam and chlormethiazole were studied for 1 week in order to elucidate if the changes observed in old age are sufficient to warrant a change in the dose or the drug given to the patient. Concern is expressed over the administration of a drug such as an hypnotic that is given over a prolonged period that may result in unduly high plasma levels of parent compound or active metabolite in the aged patient and therefore be the cause of an increased and totally unnecessary risk to the patient. 97 references.

002263 Wolf, Charles R.; Buscemi, Jon H.; Branch, Clinton E., Jr. Neurology Service, Walter Reed Army Medical Center, Washington, DC 20012 **Anticonvulsant therapy with oral paraldehyde.** *Annals of Neurology*. 6(6):554, 1979.

A case in which oral paraldehyde was successfully administered in the chronic management of epilepsy is reported. Despite various combinations of phenytoin, phenobarbital, ethosuximide, clonazepam, acetazolamide, and sodium valproate, a 44-year-old woman sustained progressive decline in her seizure control. Within 24 hours after treatment with paraldehyde the patient became alert, oriented, and without evidence of seizure activity. A continued oral regimen of paraldehyde provided almost complete freedom from seizures. When paraldehyde was tapered, the previously high frequency of attacks resumed. The patient currently receives 10ml of paraldehyde in 30ml of orange juice every 4 hours. It is reported that this regimen provides excellent control, with zero to one petit-mal seizure per day and no grand-mal attacks. 6 references.

002264 Wood, James H.; Hare, Theodore A.; Glaeser, Bruce S.; Ballenger, James C.; Post, Robert M. Division of Neurosurgery, University of Pennsylvania School of Medicine, Silverstein Pavilion 5, 3400 Spruce St., Philadelphia, PA 19104 **Low cerebrospinal fluid gamma-aminobutyric acid content in seizure patients.** *Neurology*. 29(9):1203-1208, 1979.

Mean lumbar cerebrospinal fluid (CSF) GABA concentration among 21 medicated patients with intractable seizures was found to be significantly lower than that of 20 unmedicated normal volunteers. Patients with generalized tonic/clonic (grand mal) and complex partial (psychomotor) seizures had significantly lower CSF GABA concentrations than those with simple partial (focal sensory/motor) seizures. Although lumbar CSF GABA levels in seizure patients did not significantly correlate with serum concentrations of phenytoin, phenobarbital, or primidone, additional study of medication free epileptic patients may be required to evaluate the possibility of anticonvulsant drug-induced CSF GABA alterations. 68 references. (Author abstract modified)

002265 Young, Byron; Rapp, Robert; Brooks, William H.; Madauss, William; Norton, J. A. Division of Neurosurgery, Dept. of Surgery, University of Kentucky Medical Center, Lexington, KY 40563 **Posttraumatic epilepsy prophylaxis.** *Epilepsia*. 20(6):671-681, 1979.

A phenytoin anticonvulsant regimen specifically tailored for the patient with acute head injury is described. Eighty-four patients with severe head injuries with substantial risk of posttraumatic epilepsy were administered the regimen. Only 6% of these patients had seizures during the first year after injury (First week excluded); this is considerably less than the rates reported elsewhere. Only one third of these patients are known to have continued to take phenytoin after the first month, and only half of these had plasma phenytoin concentrations above the desired minimal level. The greatly reduced incidence of posttraumatic seizures in these patients, despite the low rate of long-term drug compliance, suggests that a prophylactic effect, rather than a suppressive effect, is produced. 30 references. (Author abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

002266 Atkinson, Roland M.; Green, J. DeWayne; Chenoweth, Dennis E.; Atkinson, Judith Holmes. Psychiatry Service, Veterans Administration Medical Center, Portland, OR 97201 **Portland, OR 97201 Subjective effects of nitrous oxide: cognitive, emotional, perceptual and transcendental experiences.** *Journal of Psychedelic Drugs*. 11(4):317-330, 1979.

Research on the subjective nature of subanesthetic nitrous oxide (N2O) which was administered to healthy young adult men is reported. Most Ss experienced a complex subjective experience which was difficult to describe. N2O induced mild to moderate transcendental experiences of the same type as LSD type drugs. Similarly, cognitive impairment and variability of emotional and perceptual experience from person to person were also observed. It is concluded that nitrous oxide is a lesser and incomplete psychedelic experience than LSD, and the possible role of impaired cognition and other drug actions in producing introspective effects is discussed. 35 references.

002267 Daniel, Stephen Allen. University of Minnesota **Effects of chronic methadone and tetrahydrocannabinol (THC) on temporal discrimination performance in the pigeon.** (Ph.D. dissertation). Dissertation Abstracts International. 39(9):4610-B, 1979. Ann Arbor, Univ. Microfilms No. 7906298, 129p., 1978.

The effects of tetrahydrocannabinol (THC) and chronic methadone on temporal discrimination performance in the pigeon were examined. It was found that THC at low doses of chronic methadone had profound effects on temporal discrimination especially on long duration trials. THC altered sensitivity without significantly affecting bias. This effect was attenuated at higher methadone maintenance doses. Methadone affected temporal discrimination only when changes in the maintenance dose of methadone occurred. Tolerance to THC was shown to be an

unlikely explanation for these results. Significant effects of THC were found up to pretreatment times of 6 hours. The results are discussed in terms of several alternative explanations, both behavioral and pharmacological. (Journal abstract modified)

002268 Hofmann, Albert. no address **How LSD originated.** *Journal of Psychedelic Drugs.* 11(1-2):53-60, 1979.

The story behind the creation of LSD is recounted by the chemist who first produced it. Scientific experiments with alkaloids of ergot led to the development of drugs for uterotonic and hemostatic remedies. In a series of lyseric acid investigations, lyseric acid diethylamide (LSD-25) was produced in order to obtain a circulatory and respiratory stimulant. In a series of planned self-experiments the psychedelic qualities of LSD-25 became apparent. Reactions that were noted included altered perceptions, dizziness, and dramatic changes in consciousness.

002269 Kantor, Robert E.; Dudettes, Sharon D.; Shulgin, Alexander T. Pacific Graduate School of Psychology, Palo Alto, CA **5-Methoxy-alpha-methyltryptamine (alpha,O-dimethylserotonin), a hallucinogenic homolog of serotonin.** *Biological Psychiatry.* 15(2):349-352, 1980.

The effects induced by alpha,O-dimethylserotonin (alpha,O-DMS) in six normal, adult subjects were examined. There are two outstanding features which were consistently observed and of sufficiently long duration to constitute valid properties. The first was a clear dissociation of inward feelings from outward affect. The second feature has to do with inward visual experiences of apparent destructive events whenever the eyes were closed. This took place 12 hours after the administration of the material. It is concluded that alpha,O-DMS is the most potent indolic hallucinogen yet described, and its close chemical affiliation with serotonin should allow it to serve as a valuable probe in the study of the nature of this neurotransmitter. 21 references.

002270 Mandel, Jerrold L. United States International University **Lysergic acid diethylamide (LSD-25) as a facilitating agent in psychotherapy: a phenomenological study.** (Ph.D. dissertation). Dissertation Abstracts International. 39(11):5567-B, 1979. Ann Arbor, Univ. Microfilms No. 7909584, 127p., 1977.

A phenomenological investigation of the subconscious processes, feelings, and emotions of Ss who had undergone psychoanalytic psychotherapy under the influence of LSD-25 is described. Analysis of interview data from six patients indicates that LSD-25 provides the S with an aide to psychological disinhibition, allowing the S to observe the process of psychotherapy while it is experienced, and allows investigators an understanding of subconscious processes. (Journal abstract modified)

002271 Newmann, Mary Carol. University of Maryland **Levo-alpha-acetylmethadol and methadone: a comparison of affective states and symptomatology.** (Ph.D. dissertation). Dissertation Abstracts International. 39(7):3559-B, 1979. Ann Arbor, Univ. Microfilms No. 7909921, 206p., 1978.

A comparison of affective states and symptomatology associated with the chronic administration of two drugs used in the maintenance treatment of opiate addicts, levo-alpha-acetylmethadol (LAAM) and methadone, was made on 910 male heroin addicts. The criterion measure selected for the study was the Profile of Mood State (POMS) which was modified. No significant differences were found between drug groups on the dimensions crucial to the hypothesis and it is concluded that there were no clinically important differences between LAAM and methadone patients with respect to irritability or activity. (Journal abstract modified)

002272 Shannon, Harlan E. National Institute on Drug Abuse, Division of Research, Addiction Research Center, Lexington, KY 40583 **MDA and DOM: substituted amphetamines that do not produce amphetamine-like discriminative stimuli in the rat.** *Psychopharmacology.* 67(3):311-312, 1980.

To evaluate whether 3,4-methylenedioxymphetamine (MDA) and 2,5-dimethoxy-4-methylamphetamine (DOM)(amphetamine congeners that produce both amphetamine-like and LSD-like effects) should be classed with amphetamine, their capacity to produce amphetamine-like discriminative stimuli was assessed. Rats were trained to discriminate between saline and 1.0mg/kg d-amphetamine in a two choice, discrete trial, shock avoidance paradigm. Neither MDA nor DOM produced any amphetamine appropriate responding when tested over a 30 fold dose range. The specificity of the procedure to detect amphetamine-like effects was demonstrated by the failure of LSD to produce any amphetamine appropriate responding. These results suggest that neither MDA nor DOM should be classed as amphetamine-like agents. 7 references. (Author abstract modified)

002273 Tyler, Joan; Hargreaves, William A.; Weinberg, J. Arthur. Hargreaves: University of California, 1464 Fifth Avenue, San Francisco, CA 94143 **Success and failure of LAAM maintenance: selected case studies.** *Journal of Psychedelic Drugs.* 12(1):41-46, 1980.

A series of brief case vignettes of 35 men transferred from methadone maintenance to maintenance on methadyl acetate (levo-alpha-acetylmethadol or LAAM), a derivative of methadone that is being tested as a maintenance drug for heroin addicts, is presented. It appears that LAAM is an effective maintenance drug that is as safe as methadone, and frees patients from daily clinic visits without requiring take home doses that may cause accidental overdose depths in nonaddicted individuals, or which may be sold on the black market. Ss are classified as LAAM continuers, early terminators, and later terminators, and LAAM continuers are ranked from those who seemed globally most improved to those who seemed least improved (in terms of drug abuse, social functioning, and psychological well-being). In reviewing these cases it appears that the LAAM failures complained of general dysphoric effects due either to: 1) uncontrolled withdrawal symptoms; 2) possible side effects of LAAM; or 3) complications from polydrug abuse. Anxiety, irritability, insomnia and depression were frequently mentioned symptoms, and did not lessen in response to increased dosages of LAAM. In several instances LAAM patients showed marked improvement in social functioning and a decrease in drug abuse while on LAAM. 3 references.

002274 Weissman, Albert; Milne, George M. Pfizer Inc., Groton, CT 06340 **Cannabinoids: definitional ambiguities and a proposal.** *Neurosciences and Biobehavioral Reviews.* 3(3):171-173, 1979.

The ambiguity of defining cannabinoids in botanical, chemical, and pharmacological frames of references is discussed in relation to public perception of the abuse potential of the compounds. A pharmacological definition, based on the ability of compounds to be subjectively generalized from delta9-tetrahydrocannabinol (THC), is advocated. Compounds sharing the subjective effects of THC would be classified as cannabinimimetics, regardless of their structural divergence from the prototype compound, and compounds lacking these subjective effects would not be impeded by the negative connotations of the cannabinoid label. 15 references. (Author abstract modified)

002275 Zinberg, Norman E. 11 Scott Street, Cambridge, MA 02138 **On cannabis and health.** *Journal of Psychedelic Drugs.* 11(1-2):135-144, 1979.

Some of the positive and negative health effects of cannabis or marihuana are reviewed. Marihuana is reported to reduce intraocular pressure for glaucoma patients and to relieve the nausea caused by chemotherapy for cancer patients. Initial research also indicates that anorexia nervosa patients show improved appetite after treatment with cannabis. However, the results are mixed because these patients often return to their former eating habits after they realize they have gained some weight. Other studies on marihuana show that it might cause respiratory problems and that it acts as an intoxicant. However, it is suggested that most research indicates that it is nonaddictive and nontoxic. Federal policy and law enforcement with regard to marihuana are discussed. The medical profession's role in acknowledging and accepting the use of drugs by people in a controlled manner in order to relieve anxiety and stress is considered.

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

002276 Aaltonen, Leena; Kanto, Jussi; Salo, Matti. Dept. of Pharmacology, Turku University, Turku, Finland **Cerebrospinal fluid concentrations and serum protein binding of lorazepam and its conjugate.** *Acta Pharmacologica et Toxicologica.* 46(2):156-158, 1980.

Cerebrospinal fluid concentrations and serum protein binding of lorazepam and its conjugate were determined following i.v. administration of lorazepam to surgical patients. Results revealed a low level of unconjugated lorazepam in CSF relative to its serum protein binding, indicating a slow and incomplete penetration through the blood/CSF barrier. The penetration of the less lipophilic conjugate was even more erratic. These findings may explain the difference in the onset of drug action observed when lorazepam is compared with other benzodiazepine derivatives. 14 references.

002277 Alebic-Kolbah, Tanja; Kajfez, Franjo; Rendic, Slobodan; Sunjic, Vitomir; Konowal, Andrzej; Snatzke, Gunther. Dept. of Biochemical and Biomedical Research, CRC, Chemical Research Company, I-33048 San Giovanni al Natone, Italy **Circular dichroism and gel filtration study of binding of prochiral and chiral 1,4-benzodiazepin-2-ones to human serum albumin.** *Biochemical Pharmacology.* 28(16):2457-2464, 1979.

Circular dichroism and gel filtration were used to study the binding of chiral and prochiral benzodiazepines to human serum albumin. Binding data for diazepam, desmethyldiazepam, and 3-methyl derivatives are given. The chiroptical properties of binding processes of prochiral and chiral benzodiazepines are discussed. 57 references. (Author abstract modified)

002278 Allen, Marcia Divoll; Greenblatt, David J.; Harmatz, Jerold S.; Shader, Richard I. Greenblatt: Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Single-dose kinetics of prazepam, a precursor of desmethyldiazepam.** *Journal of Clinical Pharmacology.* 19(8-9,Part1):445-450, 1979.

Single dose kinetics of prazepam, a precursor of desmethyldiazepam (DMDZ), were examined in 12 healthy volunteers. Multiple plasma samples drawn during 7 days following a 20mg oral dose were analyzed by electron capture gas/liquid chromatography. DMDZ was the only active unconjugated benzodiazepine detected, measurable amounts of intact prazepam or hydroxylated metabolites were not present. Peak DMDZ plasma levels averaged 138 ng/ml and time of peak concentrations ranged from 2.5 to 72 hours. First order appearance of DMDZ was demonstrated in only six subjects; in the other six subjects, a sustained absorption pattern was observed. The elimination

half life of DMDZ is long and was found to vary considerably among individuals. 13 references.

002279 Amsterdam, J. D.; Winokur, A.; Mendels, J.; Caroff, S. Dept. of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104 **Effect of gonadotropin-releasing hormone on depressed mood.** *Lancet.* No. 8152:1138, 1979.

The effect of gonadotropin releasing hormone on depressed mood was investigated in 30 depressed patients and 23 normal control Ss. In contrast to the findings of German and Stampfer no mood changes were observed in patients or controls after intravenous injection of either gonadotropin releasing hormone or placebo. Neither patients nor controls could identify the difference between the two injections, and there were no adverse reactions to gonadotropin releasing hormone. 3 references.

002280 Arora, Ramesh C.; Meltzer, Herbert Y. Illinois State Psychiatric Institute, 1601 West Taylor Street, Chicago, IL 60612 **A method for determining serotonin uptake in human platelets.** (Unpublished paper). Research Report, NIMH Grant 5R01-MH-30059, 1979. 11 p.

Effects of various experimental conditions on serotonin (5-HT) uptake in human platelets were examined in an experimental design which allowed the evaluation of the effect of diffusion and other nonsaturable processes on the affinity and maximum activity of the membrane pump for 5-HT uptake. Total 5-HT uptake was determined by incubating platelet rich plasma (PRP) with increasing concentrations of 5-HT at 37 degrees Celsius for 4 minutes. The passive uptake was measured by the addition of various 5-HT concentrations to PRP in buffer at 37 degrees Celsius, followed by immediate transfer to an ice cold water bath. The difference between the total and passive uptake was considered to be active uptake. The rate of active uptake was linear for 6 minutes. The affinity (K_m) for active platelet 5-HT uptake was 0.45 plus or minus 0.09mM and maximal rate of uptake (V_{max}) was 107 plus or minus 21pM/2x10 to the seventh power platelets/5 minutes. The described method provides a convenient and reliable measure of active 5-HT uptake suitable for clinical investigations. 20 references. (Author abstract)

002281 Arora, Ramesh C.; Meltzer, Herbert Y. Illinois State Psychiatric Institute, 1601 West Taylor St., Chicago, IL 60612 **Muscle cholinesterase: effect of phencyclidine and ketamine on rat and human muscle cholinesterase activity.** *Experimental Neurology.* 67(1):1-10, 1980.

The effects of phencyclidine (PCP) and ketamine on rat skeletal muscle acetylcholinesterase (AChE) activity and the effects of PCP on AChE activity of skeletal muscle from schizophrenic and normal subjects were studied. Both drugs weakly inhibited rat skeletal muscle AChE activity and human muscle AChE activity in vitro. In vivo, both drugs stimulated rat skeletal muscle AChE activity whereas no effect was observed on rat brain AChE activity. When combined with restraints for 30 min following PCP and ketamine, the stimulation of AChE activity was greater than that produced by drug alone or restraint alone. No difference in the ability of PCP to inhibit AChE activity of skeletal muscle from schizophrenic patients compared to normal controls was noted. 25 references. (Author abstract modified)

002282 Belmaker, Robert H.; Kon, Mario; Ebstein, Richard P.; Dasberg, Haim. Dept. of Research, Jerusalem Mental Health Center -- Ezrath Nashim, Jerusalem, Israel **Partial inhibition by lithium of the epinephrine-stimulated rise in plasma cyclic GMP in humans.** *Biological Psychiatry.* 15(1):3-8, 1980.

The partial inhibition by lithium of the epinephrine stimulated rise in plasma cyclic GMP was investigated in humans. Lithium treated and drug free individuals were each given 0.5mg epin-

ephrine subcutaneously and blood samples were withdrawn for measurement of plasma cyclic AMP and cyclic GMP. The rise in plasma cyclic GMP in response to epinephrine was found to be partially inhibited by lithium treatment, and previous reports of lithium inhibition of the plasma cyclic AMP rise were replicated. Effects of lithium on cyclic AMP and cyclic GMP may relate to lithium's biphasic efficacy in depression and mania. 14 references. (Author abstract modified)

002283 Bental, E.; Lavie, P.; Sharf, B. Unit of Behavioral Biology, Gutwirth Building, Technion-Israel Institute of Technology, Haifa, Israel **Severe hypermotility during sleep in treatment of cataplexy with clomipramine.** *Israel Journal of Medical Sciences.* 15(7):607-609, 1979.

A case study of a 52-year-old man who suffered from narcolepsy with marked cataplexy is described. Clomipramine hydrochloride effectively controlled the cataplexy and partially alleviated the daytime sleep attacks. However, clomipramine treatment resulted in episodes of severe motor hyperactivity during sleep, which were most intense during rapid eye movement sleep. 12 references. (Author abstract)

002284 Bonnet, Michael H.; Webb, Wilse B. Naval Regional Medical Center, San Diego, CA 92134 **Sleep studies following repeated awakenings./ The return to sleep.** *Biological Psychology.* 8(3):225-233, 1979.

The latency of return to sleep following repeated awakenings was investigated as a function of pentobarbital, flurazepam, and caffeine. Six young adult Ss were awakened five to eight times per night from stage 2 sleep in a standardized manner for a series of at least 11 nonconsecutive nights. After adaptation to the procedure, Ss received placebo, pentobarbital, or flurazepam on two random nights and caffeine on one night. On placebo nights a characteristic U-shaped curve of latency as a function of time of night was found. Latencies were long shortly after sleep onset but decreased rapidly to about 50 sec before beginning an approximately linear logarithmic increase throughout the rest of the night. The drugs characteristically altered this time course. Pentobarbital decreased latencies in the first half of the night. Flurazepam decreased latencies throughout the night. Caffeine increased latencies during the first half of the night. 23 references. (Author abstract modified)

002285 Brewster, David; Muir, Neil C. Dept. of Drug Metabolism, Reckitt and Colman, Pharmaceutical Division, Dansom Lane, Hull, North Humberside, England **Valproate plasma protein binding in the uremic condition.** *Clinical Pharmacology and Therapeutics.* 27(1):76-82, 1980.

Equilibrium dialysis was used to study the protein binding of sodium (carboxy-¹⁴C)valproate in plasma from uremic patients and from normal Ss. Protein binding was dependent on concentration in both cases, but a marked reduction in binding capacity was seen in patients with renal dysfunction. Treatment of normal plasma with urea or creatinine to reproduce concentrations observed in uremia resulted in small decreases in binding. Diffusion dialysis of uremic plasma partially restored the degree of binding. Pretreatment of uremic plasma with activated charcoal at pH 3 raised binding capacity to that of normal plasma. 29 references. (Author abstract modified)

002286 Briley, Michael S.; Raisman, Rita; Langer, S. Z. Dept. of Biology, Synthelabo L.E.R.S., 58, rue de la Glacière, F-75013 Paris, France **Human platelets possess high-affinity binding sites for 3H-imipramine.** *European Journal of Pharmacology.* 58(3):347-348, 1979.

The binding of tritiated imipramine to membranes from rat cerebral cortex and human platelets was examined. The platelet

membranes had a slightly higher affinity for 3H-imipramine than rat cortex membranes, and maximal binding was much greater in platelets. Studies with a series of 12 drugs revealed virtually identical inhibition of 3H-imipramine binding to the cortex and platelet membranes. Studies of the specific high affinity binding of 3H-imipramine to human platelet membranes in normal and depressed patients may be useful in the diagnosis and treatment of depression. 4 references.

002287 Brinkschulte, Maria; Breyer-Pfaff, Ursula. Breyer-Pfaff: Institut für Toxikologie, Universität Tübingen, Wilhelmstrasse 56, D-7400 Tübingen, Germany **Binding of tricyclic antidepressants and perazine to human plasma: methodology and findings in normals.** *Naunyn-Schmiedeberg's Archives of Pharmacology.* 308(1):1-7, 1979.

The binding of amitriptyline (AT), nortriptyline (NT), imipramine (IP), desmethylimipramine (DMI), and perazine (PER) to plasma from healthy volunteers was measured by equilibrium dialysis at 37 degrees C. Binding values were not dependent on age or sex, and no differences between female users of sexual hormones and nonusers were detected. A significant negative correlation was established between plasma total cholesterol and the free fractions of AT, NT, DMI, and PER. Corresponding alterations were observed within individuals when cholesterol levels fluctuated within several weeks or months. The phospholipid concentration in plasma did not correlate with drug binding. The concentration dependence of AT and NT binding pointed to the contribution of plasma constituents present in low concentrations and exhibiting high affinity toward the drugs; part of these constituents may be lipoproteins. 26 references. (Author abstract modified)

002288 Bukowczyk, Adam; Pionkowski, Janusz; Szefer, Andrzej; Zaleski, Ryszard. Klinika Psychiatria AM, ul. Aleksandrowska 159, 91-229 Lodz, Poland **Red blood cells of patients treated with neuroleptics./ Krwinki czerwone u chorych leczonych neuroleptykami.** *Psychiatria Polska.* 13(2):97-101, 1979.

The structure of erythrocytes in the blood of male mental patients treated with neuroleptics was studied. A statistical analysis of the results of study of 118 patients treated in 1976 to 1977, including 105 schizophrenics, shows a clear difference between the patients treated with neuroleptics over long periods of time and the control group of 99 healthy blood donors, a slight difference between patients treated with chlorpromazine and various neuroleptics, and an even smaller difference between patients treated over a long period with chlorpromazine and healthy persons. It is concluded that prolonged treatment with various neuroleptics causes a decrease in the hematocrit ratio and hemoglobin level in blood to a much greater extent than does prolonged treatment with chlorpromazine alone. These decreases and the decrease in the number of erythrocytes do not go below the limit of the value considered as normal. 10 references. (Journal abstract modified)

002289 Calvo, R.; Carlos, R.; Erill, S. Dept. of Pharmacology, School of Medicine, Universidad de Bilbao, Lejona, Spain **Etomidate and plasma esterase activity in man and experimental animals.** *Pharmacology.* 18(6):294-298, 1979.

The interaction of the hypnotic drug etomidate and plasma esterase was examined in humans and in several animal species. No hydrolysis of etomidate in plasma was observed in vitro in samples from humans, horses, cows, sheep, guinea-pigs, or white rabbits. Hydrolysis was moderate in brown rabbits and marked in Wistar rats; in rats, a single enzyme (an alsesterase) participated in the hydrolysis in plasma. Etomidate did not interfere with the hydrolysis of procaine by plasma

pseudocholinesterase in humans. 14 references. (Author abstract modified)

002290 Cazzullo, Carlo L.; Smeraldi, E. Istituto di Clinica Psichiatrica, Università di Milano Milan, Italy **HLA system, psychiatry and psychopharmacology**. Progress in Neuro-Psychopharmacology. 3(1-3):137-146, 1979.

The relationships among the HLA system, psychiatric disorders, and psychotropic drugs are reviewed. Research findings of significant associations between a number of antigens of the HLA system and clinical phenotypes of schizophrenia and manic depressive disorders are noted, and directions for future research are suggested. The hypothesis that HLA determinants interfere with the interaction between neurotransmitters and/or psychotropic drugs and specific receptors is discussed, and clinical implications of HLA/A1 reactions to chlorpromazine and haloperidol, and of the HLA/A1 crossreacting antigens are analyzed. 26 references. (Author abstract modified)

002291 Chapron, Dennis J.; Kramer, Paul A.; Mariano, Sandra L.; Hohnadel, David C. Dept. of Pharmacy, University of Connecticut Health Center, Farmington, CT 06032 **Effect of calcium and antacids on phenytoin bioavailability**. Archives of Neurology. 36(7):436-438, 1979.

The effects of bihourly administration of gluconate calcium and two magnesium/aluminum containing antacids on the bioavailability of a single capsule dose of phenytoin sodium were determined in two normal volunteers. Neither the rate nor the extent of phenytoin absorption were altered by the treatments, in spite of indirect evidence from other studies that suggests such an interaction. No interaction between calcium or magnesium and either unionized or anionic phenytoin could be demonstrated in vitro using solubility and spectral techniques. 13 references. (Author abstract modified)

002292 Cole, Jonathan O.; Gardos, George. Boston Mental Health Foundation, Inc., Boston, MA **The treatment of persistent dyskinesias**. (Unpublished paper). Final Report, NIMH Grant R01-MH-27505, 1979. 8 p.

Newer drug treatments for tardive dyskinesia (TD) (clozapine, cyproheptadine, papaverine, clonazepam, L-dopa with carbidopa) were evaluated, and a new multi item scale (Dyskinesia Rating Scale) was developed and refined. The potential use of an antiparkinson drug, benztropine, in uncovering dyskinesia was explored in a double-blind placebo controlled trial. A 12 year followup study of 124 chronic psychotic patients was conducted to assess dyskinesia and psychosocial adjustment in diverse community settings. The followup study revealed that patients currently residing in cooperative apartments, family care homes, or rented rooms or apartments function significantly better than patients in mental hospitals, nursing homes, or those living with their families. These differences extend over a wide range of measures such as psychopathology, social behavior, work adjustment, and level of dyskinetic movements. The overall results tend to support the concept of TD as a heterogeneous entity with multiple etiological factors and diverse clinical manifestations. 15 references.

002293 Coleman, Mary; Steinberg, Grace; Tippet, Jean; Bhagavan, Hemmige N.; Coursin, David Baird; Gross, Marion; Lewis, Carol; DeVeau, Leslie. no address **A preliminary study of the effect of pyridoxine administration in a subgroup of hyperkinetic children: a double-blind crossover comparison with methylphenidate**. Biological Psychiatry. 14(5):741-751, 1979.

A small sample of six patients with the putative syndrome participated in a research protocol comparing administration of pyridoxine, methylphenidate, and placebos. The children had

had low whole blood serotonin levels and a history of previous responsiveness to methylphenidate. Results of the double-blind clinical evaluation showed trends suggesting that both pyridoxine and methylphenidate were more effective than placebo in suppressing the symptoms of hyperkinesia. Pyridoxine elevated whole blood serotonin levels, methylphenidate did not. Clinical and laboratory evidence indicated that the pyridoxine effects persisted after the 3 week period when the vitamin had been given. 28 references. (Author abstract)

002294 Davis, Bonnie M.; Davis, Kenneth L. Psychiatric Clinical Research Center, Veterans Administration Medical Center, Palo Alto, CA **Cholinergic mechanisms and anterior pituitary hormone secretion**. Biological Psychiatry. 15(2):303-310, 1980.

The effect of physostigmine on anterior pituitary hormone secretion in 17 normal male subjects was examined in an attempt to identify a hormone whose levels would reflect central cholinergic transmission. Methscopolamine was given to partially block the visceral effects of physostigmine. Methscopolamine did not affect secretion of cortisol, prolactin, growth hormone, or luteinizing hormone. The dose of physostigmine did not bear an obvious relationship to resulting hormone concentrations. It was not possible to identify an anterior pituitary hormone whose level could reflect changes in central cholinergic activity. 29 references.

002295 Dorus, Elizabeth; Pandey, Ghanshyam N.; Shaughnessy, Rita; Davis, John M. Dept. of Psychiatry, University of Chicago, 950 East 59th Street, Chicago, IL 60637 **Lithium transport across the RBC membrane: a study of genetic factors**. Archives of General Psychiatry. 37(1):80-81, 1980.

Lithium transport across the RBC membrane was studied in vitro in 291 members of 120 families. No significant effects of age, sex, ethnic origin, or SES on the ratio of RBC to plasma lithium ion levels were found. Between family variance was significantly greater than the within family variance, and the parent/offspring and sibling/sibling correlations did not differ significantly from .50 and were significantly greater than zero, suggesting that genetic factors play a substantial role in the distribution of lithium ions across the RBC membrane. Results are discussed in relation to studies of lithium ion transport in the pathogenesis of affective disorders and in response to lithium treatment. 18 references. (Author abstract modified)

002296 Ellingboe, James; Mendelson, Jack H.; Kuehnle, John C. Alcohol and Drug Abuse Research Center, McLean Hospital, Belmont, MA 02178 **Effects of heroin and naltrexone on plasma prolactin levels in man**. Pharmacology Biochemistry and Behavior. 12(1):163-165, 1980.

The effects of heroin and naltrexone on plasma prolactin levels in man were investigated. Plasma levels of prolactin were increased following intravenous self-administration of heroin by young men with a history of heroin addiction. Following 10 days of controlled heroin usage, tolerance could be demonstrated to the acute prolactin releasing effect of heroin. There was no evidence that a single dose of naltrexone affected basal prolactin levels. 27 references. (Author abstract modified)

002297 Gold, Philip W.; Extein, Irl; Ballenger, James C.; Wehr, Thomas A. Unit on Neuroendocrinology, Clinical Psychobiology Branch, NIMH, Building 10, Rm. 4S239, 9000 Rockville Pike, Bethesda, MD 20205 **Rapid mood cycling and concomitant cortisol changes produced by cyproheptadine**. American Journal of Psychiatry. 137(3):378-379, 1980.

A placebo controlled, double-blind therapeutic trial of cyproheptadine was conducted in a 41-year-old female inpatient with bipolar affective disorder. After the patient went through a

period of depression on placebo, she was administered 4mg/day cyproheptadine, which was gradually raised to 24mg/day over the next 18 days. On the 37th day of cyproheptadine treatment, the patient switched into a 3 day hypomania. Over the next 32 days, she had six complete cycles of depression followed by mania. Manias lasted 2 to 3 days and were characterized by hyperactivity, talkativeness, sexual preoccupation, increased appetite and decreased sleep. Depressions lasted 1 to 5 days and were characterized by profound retardation, hypersomnia, suicidality, and some catatonic features. From day 79 of treatment to day 118 she remained depressed despite an increase in dosage to 32mg/day. Urinary free cortisol (UFC) was consistently higher during depression than during mania. A premonitory rise in UFC was noted on the day before each switch from mania into depression; and UFC levels also tended to fall before the switch from depression into mania. Results correspond with the theory that depressions associated with hypothalamic/pituitary/adrenal axis activation are related to increased central serotonergic function, and are also consistent with the suggestion that mania occurs when the inhibitory influence of the serotonergic raphe neurons on the hippocampus is removed. 10 references.

002298 Gold, Philip W.; Goodwin, Frederick K.; Ballenger, James C.; Weingartner, Herbert; Robertson, Gary L.; Post, Robert M. Clinical Psychobiology Branch, NIMH, Bethesda, MD 20205 Central vasopressin function in affective illness. (Unpublished paper). Bethesda, MD, NIMH, 1979. 21 p.

Preliminary findings, which show that in drug free manic-depressive patients, both the cerebrospinal fluid levels of arginine vasopressin (AVP) and the plasma AVP response to hypertonic saline is reduced in depression compared with mania, are reported. When depressed patients were given sustained administration of 1-deamin-D-arginine vasopressin (DDAVP), a synthetic analogue of AVP, some showed enhancements of cognitive function and amelioration of depressive symptomatology. These findings are compatible with an hypothesis of relatively diminished AVP function in depression compared with mania. 16 references. (Author abstract)

002299 Halton, David M. Wayne State University School of Medicine, Metabolic Service, Dept. of Pediatrics, Children's Hospital of Michigan, Detroit, MI 48201 D-Glucose transport in erythrocytes and synaptosomes -- a comparison of the effects of three centrally acting drugs. Biochemical Pharmacology. 28(15):2399-2401, 1979.

To determine the usefulness of erythrocytes as models for drugs actions on D-glucose transport in nerve facilitated systems, the effects of chlorpromazine, mescaline, and secobarbital on D-glucose transport systems of rat brain cortex synaptosomes and human erythrocytes were compared. Chlorpromazine and mescaline inhibited glucose transport in both preparations. Secobarbital stimulated glucose uptake into synaptosomes, but had no apparent effect in erythrocytes. Results indicate that failure of a test drug to alter the human erythrocyte transport system does not rule out the possibility of an influence on D-glucose transport in synaptosomes. 24 references.

002300 Ho, W. K. K.; Wen, H. L.; Ling, N. Addiction Research Foundation, 701 Welch, Palo Alto, CA 94304 Beta-endorphin-like immunoactivity in the plasma of heroin addicts and normal subjects. Neuropharmacology. 19(1):117-120, 1980.

The plasma beta-endorphin levels of heroin addicted and normal Ss were measured by radioimmunoassay. The mean assayable beta-endorphin activity in the addicted group (345pg/ml) was significantly lower than that in normal Ss (1024pg/ml). This finding is consistent with the proposal that chronic endor-

phin deficiency may be the underlying cause of chronic heroin addiction. 8 references. (Author abstract modified)

002301 Hyyppa, Markku T.; Jolma, Tapani; Liira, Juha; Langvik, Vivi-Ann; Kytomaki, Ossi. Third Clinical Institute, University of Turku, SF-20520 Turku 52, Finland L-tryptophan treatment and the episodic secretion of pituitary hormones and cortisol. Psychoneuroendocrinology. 4(1):29-35, 1979.

Plasma free and total tryptophan, somatotropin, follitropin (FSH), lutropin (LH), prolactin, and cortisol levels were determined in normal Ss after oral administration of 2g or 100mg/kg L-tryptophan or 1.28g L-leucine at 8:30 and 11:30 a.m. Oral administration of L-tryptophan significantly elevated plasma levels of free and total tryptophan and of somatotropin. Pulsatile secretion of FSH and LH was not affected by L-tryptophan or L-leucine and plasma prolactin was not elevated. A significant morning decline in plasma cortisol levels was observed with or without L-tryptophan treatment, but no decline was observed after L-tryptophan administration in the middle of the day. 22 references. (Author abstract modified)

002302 Jayasundar, S.; Vohra, M. M. Dept. of Pharmacology, Madras Veterinary College, Madras 600 007, India Recent studies of the actions of cholinomimetic drugs on adrenergic nerves and their implications for the cholinergic link hypothesis. Canadian Journal of Physiology and Pharmacology. 58(1):1-6, 1980.

The results of recent studies of the actions of cholinomimetic drugs on adrenergic nerve terminals and their implications for the cholinergic link hypothesis are analyzed. Thus far, evidence suggests that the only possible action of endogenous acetylcholine (ACh) present near noradrenaline (NA) stores is an inhibition of the release of NA from the adrenergic nerve terminals and that NA is released only when the action of acetylcholinesterase is inhibited. Nicotinic agents have been shown to act on adrenergic nerve terminal membranes, a finding that casts doubt on the proposed intraneuronal cholinergic sites for the action of endogenous ACh. Current findings do not support the proposal that nicotinic agents in higher concentrations interfere with adrenergic neurotransmission. It is concluded that nicotinic agents, in causing the release of NA from adrenergic nerve terminals, are merely exhibiting a pharmacological action and not mimicking the physiological function of ACh, as proposed by the cholinergic link hypothesis. 46 references. (Author abstract modified)

002303 Knoll, J. Dept. of Pharmacology, Semmelweis University of Medicine, 1085 Budapest, Ulloi ut 26, Hungary Azidomorphines: a new family of potent analgesics with low dependence capacity. Progress in Neuro-Psychopharmacology. 3(1-3):95-108, 1979.

Structure/activity relationship studies with new semisynthetic isomorphine derivatives which indicate that substitution of an azido group in position 6 (azidomorphines) greatly increases the analgesic potency while tolerance and dependence liability decrease, are reviewed. Experiments with mice, rats, and rhesus monkeys indicate that azidomorphine (6-deoxy-6-azidodihydroisomorphine) and 14-hydroxyazidomorphine (6-deoxy-6-azidodihydro-14-hydroxyisomorphine) are the most effective analgesics among the semisynthetic morphine alkaloids. The azidomorphine and rymazolium (Probon) combination was found to be less respiratory depressant in humans than azidomorphine administered alone. In patients with chronic intractable pain, an association of azidomorphine and rymazolium achieved total pain relief without noticeable euphoria and none of the twelve patients showed acute abstinence syndromes after nalorphine administration (Himmelsbach scoring system). 43 references. (Author abstract modified)

002304 Kober, Anita; Sjöholm, Ingvar; Borga, Olof; Odar-Cederlof, Ingegerd. Sjöholm: Dept. of Pharmaceutical Biochemistry, BMC, Box 578, S-751 23 Uppsala, Sweden **Protein binding of diazepam and digitoxin in uremic and normal serum.** *Biochemical Pharmacology*. 28(7):1037-1042, 1979.

The protein binding of diazepam and digitoxin in serum from uremic patients was studied by equilibrium dialysis and compared to that in normal serum and in isolated human serum albumin (HSA) from uremic and normal Ss. The binding of diazepam and digitoxin was impaired in serum from patients compared to normal serum, due to decreased affinity for their respective primary binding sites on albumin. The number of binding sites for diazepam was greater in uremic serum than in normal serum and HSA. The number of digitoxin binding sites was larger in normal and patient serum than in HSA. The binding of both drugs was improved after charcoal treatment of the uremic albumin at pH 3.0. 27 references. (Author abstract modified)

002305 Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Catecholamines and blood pressure regulation.** (Unpublished paper). Bethesda, MD, NIMH, 1979. 29 p.

Data are presented to show that, although many biogenic amines have powerful actions on vascular smooth muscle, only the catecholamines, by their effect on renin production as well as by their direct cardiovascular actions, play a significant role in blood pressure regulation via actions outside of the brain. The catecholamines in the brain, and perhaps other amine neurotransmitters, appear to be involved in mechanisms for the central regulation of blood pressure. Drugs which interfere with synthesis, storage, release, receptor activation, or termination of activity of catecholamines later aminergic neurotransmission. Enzymes which control catecholamine biosynthesis are discussed: tyrosine hydroxylase, aromatic amino acid decarboxylase, dopamine-beta-hydroxylase, and phenylethanolamine-N-methyltransferase. Blood pressure regulation is discussed in terms of: baroreceptors and reflexes; and catecholamines and hypertension (sympathetic nervous system and the central nervous system and antihypertensive drugs). Also discussed are: catecholamine storage and release, disposition and metabolism of catecholamines, and adrenergic receptors. 76 references.

002306 Kotzan, Jeffrey A.; Needham, Thomas E.; Honigberg, Irving L.; Vallner, Joseph J.; Stewart, James T.; Brown, Walter J.; Jun, Hung W. Biological Group Studies, School of Pharmacy, University of Georgia, Athens, GA 30602 **Examination of blood clobazam levels and several pupillary measures in humans.** *Journal of Pharmaceutical Sciences*. 68(8):1002-1004, 1979.

The effects of clobazam on cognitive and noncognitive pupillary measures (constriction, dilation, and critical flicker fusion) were determined in 15 healthy male volunteers divided into three groups on the basis of scores on the State-Trait Anxiety Inventory. Results showed that pupil diameter was reduced when blood levels of the drug and its metabolite peaked. However, pupil diameters did not remain constricted at the 6 hour point when blood levels exceeded 350ng/ml. Anxiety state was correlated with the drug effects on the cognitive pupillary measure. 18 references. (Author abstract modified)

002307 Krieger, Dorothy T.; Liotta, A. S.; Brownstein, M. J.; Zimmerman, E. A. Department of Medicine, Division of Endocrinology, Mount Sinai School of Medicine, New York, NY 10029 **ACTH, beta-lipotropin and related peptides in brain, pituitary and blood.** (Unpublished paper). Bethesda, MD, NIMH, 1979. 109 p.

Information available with regard to the nature and regulation of extrapituitary forms of the adrenocorticotrophic hormone

(ACTH) secreted by the human pituitary, both in normal subjects and in diseases characterized by disorders of ACTH regulation, is presented. Areas covered are: 1) the ACTH precursor molecule; 2) ACTH related peptides in anterior and intermediate pituitary lobe; 3) central nervous system (CNS) ACTH related peptides (demonstration and quantitation, immunocytochemical studies, evidence for CNS site of origin, is there a pituitary source of CNS ACTH related peptides, regulation and function of CNS ACTH related peptides); and 4) placental ACTH and related peptides (demonstration and quantification, evidence for placental synthesis, physiological role of placental ACTH and related peptides). Also covered are: 1) gastrointestinal tract ACTH-like peptides, and 2) plasma ACTH and peptides (studies in normal subjects, studies in patients with pituitary adrenal disease). 188 references.

002308 Kugler, Barbara T.; Gruzelier, John H. Dept. of Psychiatry, Gruzelier: Charing Cross Hospital Medical School, Fulham Place Rd., London W6 8RF, England **The influence of chlorpromazine and amylobarbitone on the recovery limb of the electrodermal response.** *Psychiatry Research*. 2(1):75-84, 1980.

To examine the effects of chlorpromazine and amylobarbitone on the recovery limb of the electrodermal response, 12 healthy normal subjects were administered single oral doses of chlorpromazine, amylobarbitone, and a placebo in a double-blind, latin square design. Skin conductance was recorded bilaterally from bipolar placements of silver/silver chloride cup electrodes. Skin conductance ordering responses were examined to 13 tones of 1000 Hz presented at variable intervals. Results show that chlorpromazine, but not amylobarbitone, influenced the slope of the recovery limb of responses to simple oriented stimuli with no signal significance. Results detract from existing evidence that the slope of the recovery limb of the electrodermal response is an indicator of schizophrenia. 26 references.

002309 Kulhanek, F.; Linde, O. K.; Meisenberg, G.; Hirsch, Steven R. Dept. of Psychiatry and Psychopharmacology, von Heyden GmbH Squibb, D-800 Munich 19, Germany **Precipitation of antipsychotic drugs in interaction with coffee or tea.** *Lancet*. No. 8152:1130-1131, 1979.

The interactions of antipsychotic drugs with coffee and tea are discussed in the context of pharmacodynamics of central activity, and a demonstration of the precipitation of fluphenazine, haloperidol, phenothiazine, and butyrophenone drops by coffee and tea is described. Analysis of the supernatant solutions and sediments suggest that about 10% of the drug was precipitated, bound, or otherwise changed in coffee and about 90% in tea. The relationship between these findings and the often noted variation in plasma concentrations of antipsychotic drugs is discussed. 11 references.

002310 Lal, S.; Mendis, T.; Cervantes, P.; Guyda, H.; DeRiviera, J. L. Dept. of Psychiatry, Montreal General Hospital, Montreal, Quebec, Canada H3G 1A4 **Effect of benztropine on haloperidol-induced prolactin secretion.** *Neuropsychobiology*. 5(6):327-331, 1979.

The effect of benztropine on haloperidol-induced prolactin secretion was investigated in 10 normal male volunteers. Benztropine had no effect on basal prolactin secretion but significantly enhanced the increase induced by haloperidol. The magnitude of the enhancement, however, was relatively small. These data suggest that, in man cholinergic mechanisms have no effect on basal prolactin secretion but exert a weak inhibitory effect under conditions of dopamine receptor blockade. Differences in intrinsic anticholinergic properties may account for some of the variations in potency of different neuroleptics in increasing circulating prolactin concentrations. 20 references. (Author abstract)

002311 Lerk, C. F.; Lagas, M.; Lie-A-Huen, L.; Broersma, P.; Zuurman, K. Laboratory for Pharmaceutical Technology, University of Groningen, Antonius Deusinglaan 2, 9713 AW Groningen, The Netherlands *In vitro* and *in vivo* availability of hydrophilized phenytoin from capsules. *Journal of Pharmaceutical Sciences*. 68(5):634-638, 1979.

The effect of phenytoin hydrophilization on the liquid penetration rate into prepared plugs, on the disintegration time, on the *in vitro* release rate, and on *in vivo* absorption in humans was studied. Hydrophilization was performed by intensive mixing of the hydrophobic drug with a small amount of methylcellulose solution. Liquid penetration into the treated plugs was independent of the liquid wetting potency and extremely high compared to the pure drug plugs. Analogous results were obtained for the disintegration time and *in vitro* release rates from capsules loaded with pure and treated drug. A bioavailability study in seven healthy volunteers showed immediate absorption of the treated drug, compared to a 1 hour absorption lag time for the pure drug. 18 references. (Author abstract)

002312 Lieberman, Abraham N.; Leibowitz, Morton; Neophytides, Andreas; Kupersmith, Mark; Mehl, Sidney; Kleinberg, David; Serby, Michael; Goldstein, Menek. New York University School of Medicine, New York, NY 10016 *Pergolide and lisuride for Parkinson's disease*. *Lancet*. No. 8152:1129-1130, 1979.

Clinical trials of a synthetic ergoline (pergolide mesylate, and a semisynthetic ergoline (lisuride hydrogen maleate) in the treatment of 28 Parkinson's disease patients are reported. Pergolide, when added to levodopa, had a dramatic effect in 13 nonambulatory inpatients with advanced Parkinson's disease, including seven with on/off features who were no longer responding to levodopa and bromocriptine. Lisuride, when added to levodopa, had a marked effect in 15 patients (mostly outpatients), including seven with on/off responses. Both drugs are seen as promising new antiparkinsonian agents. Lisuride seems to induce less orthostatic hypotension and less involuntary movement than does pergolide. 15 references.

002313 Lieberman, K. W.; Stokes, P. E.; Kocsis, J. Department of Biochemistry, Cornell University Medical College, New York, NY *Characteristics of the uptake of lithium isotopes into erythrocytes*. *Biological Psychiatry*. 14(5):845-849, 1979.

An investigation of the possibility that the minor lithium isotope $Li6$ was differentiable from the major isotope $Li7$ is reported. An *in vitro* lithium uptake procedure utilized erythrocytes derived from a mixed population of subjects consisting of psychiatric normals, manic-depressives, and primary alcoholics of both sexes who were not receiving lithium as a medication. The difference in the quantity of $Li6$ or $Li7$ that entered the erythrocyte as a function of time was examined. The quantity of $Li6$ which entered the erythrocyte was found to be greater than the amount of $Li7$ with the ratio of the concentrations of $Li6/Li7$ in the erythrocyte ranging from 1.054 to 1.085. The physicochemical properties of lithium are discussed. It is concluded that potentially important differences in the physicochemical properties of the lithium isotopes are present, but that their specific relationship to the observed differences in the quantities of $Li6$ or $Li7$ which entered the erythrocyte is not clear at this time. 15 references.

002314 Linnolia, M.; Viukari, M.; Vaisanen, K.; Auvinen, J. Dept. of Psychiatry, Duke University Medical Center, Durham, NC 27710 *Plasma neuroleptic and prolactin levels in mentally retarded patients*. *Acta Pharmacologica et Toxicologica*. 46(2):159-160, 1980.

Plasma prolactin levels were measured in 16 mentally retarded patients treated with haloperidol and thioridazine in a

double-blind crossover study. All patients showed a significant increase in plasma prolactin level during neuroleptic treatment, but this increase could not be correlated with plasma drug levels. Results suggest there may be a ceiling effect for the neuroleptic-induced plasma prolactin level increment. If so, single determinations of plasma prolactin are not adequate indicators of actual plasma neuroleptic levels during steady state kinetics. 7 references.

002315 Lucek, Rudolph; Dixon, Ross. Research Division, Hoffmann-La Roche Inc., Nutley, NJ 07110 *Chlordiazepoxide concentrations in saliva and plasma measured by radioimmunoassay*. *Research Communications in Chemical Pathology and Pharmacology*. 27(2):397-400, 1980.

A new, sensitive, and specific radioimmunoassay for chlordiazepoxide was used to determine concentrations of the drug in microsamples of saliva and plasma following intravenous or oral administration to human Ss. Saliva and plasma concentrations of the drug were highly correlated, and the saliva/plasma ratio had a mean value of about 0.03. Saliva levels of chlordiazepoxide were equal to the concentration of unbound drug in plasma. Drug half-lives determined from plasma and saliva concentration/time curves were equivalent. 5 references. (Author abstract modified)

002316 Mandell, Arnold J. Dept. of Psychiatry (M-003), University of California, San Diego School of Medicine, La Jolla, CA 92093 *On a mechanism for the mood and personality changes of adult and later life: a psychobiological hypothesis*. *Journal of Nervous and Mental Disease*. 167(8):457-466, 1979.

An overview of recent research findings in biogenic amine regulation, temporal lobe limbic neurophysiology, psychomotor epilepsy, bilateral hemisphere specialization, and the mechanisms of action of psychotropic drugs is presented. Descending and reciprocal inhibition of endogenous excitation in the brain and the reduction with aging of levels and/or rates of synthesis of biogenic amines suggest that aging may bring decreased thresholds for the emergency of neural expression. Several lines of evidence suggest that progressive disinhibition of the dominant hemisphere leads to the expression of dysphoric, obsessional, and depressive personality features. Heretofore, study of the serotonergic system in various mood related behaviors has indicated functional models representing specific information processing circuitry. A dualistic model is presented that considers the functional regulatory potential of the degree of hemispheric asymmetry in certain serotonergic systems. The implications on the affect of tricyclic drugs on the conformation of tryptophan hydroxylase are discussed. A model is proposed that suggests the usefulness of the integration of the hemispheric modalities at the neurobiological level for successful treatment at the level of subjective phenomenology. 98 references.

002317 Martinelli, P.; Montagna, P. Institute of Neurology, University of Bologna, Via Foscolo 7, I-40123 Bologna, Italy *Conditioning of the H reflex by stimulation of the posterior tibial nerve in Parkinson's disease*. *Journal of Neurology, Neurosurgery, and Psychiatry*. 42(8):701-704, 1979.

The excitability curve of the H-reflex conditioned by stimulation of a mixed nerve was studied in eight Parkinson patients, before and after L-dopa therapy. There was no significant variation between the two curves. However, there was a reduction of the normal early inhibition of the H-reflex conditioned by exteroceptive stimulation. This indicates the presence of alterations in the organization of the reflex pathways at a spinal level in this disease. 28 references. (Author abstract)

002318 Meltzer, Herbert Y.; Goode, David J.; Schyve, Paul M.; Young, Michael; Fang, Victor S. University of Chicago

Pritzker School of Medicine, 950 East 59th St., Chicago, IL 60637 **Effect of clozapine on human serum prolactin levels.** *American Journal of Psychiatry.* 136(12):1550-1555, 1979.

The effects of clozapine on serum prolactin levels were investigated. Serum prolactin levels in 13 patients receiving clozapine, an antipsychotic drug that does not produce extrapyramidal side effects, were determined. Morning serum prolactin levels, 11 hours after the last dose, were not elevated during chronic treatment with clozapine in any subject despite its therapeutic effects. Serum prolactin levels were moderately increased between 90 minutes and 4 hours after administration of very high doses of oral clozapine in 4 patients but were smaller than those produced by chlorpromazine in other subjects. It is suggested that clozapine may achieve its antipsychotic effect differently than do the classical neuroleptics, and that sustained prolactin increases are not essential for antipsychotic action. 58 references. (Author abstract)

002319 Mendlewicz, J.; Linkowski, P.; Brauman, H. Dept. of Psychiatry, Free University of Brussels, Erasme and Brugmann University Hospitals, Brussels, Belgium **TSH responses to TRH in women with unipolar and bipolar depression.** *Lancet.* No. 8151:1079-1080, 1979.

Thyroid stimulating hormone (TSH) responses to thyrotropin releasing hormone (TRH) were studied in 58 female depressive patients (31 unipolar and 27 bipolar) matched for age and sex with 42 normal female controls. Twenty-seven premenopausal (15 unipolar and 12 bipolar) and 31 postmenopausal (12 unipolar and 19 bipolar) female patients were studied during a depressive episode severe enough to warrant hospital admission. All patients were tested before, and some were tested after treatment which consisted of amitriptyline. Before treatment, the TSH response to TRH was significantly lower in the unipolar and bipolar patient than in the controls. Results indicate the importance of ovarian status in the TSH response of female patients to TRH. 4 references.

002320 Murialdo, G.; Masturzo, P.; Polleri, A.; Carolei, A.; Toffano, G. Polleri: ISMI, Viale Benedetto XV, 6, I-16132 Genoa, Italy **Lack of counteracting effect of liposomes on benserazide-induced hyperprolactinemia.** *Neuropsychobiology.* 5(6):317-321, 1979.

Research was conducted to determine if liposomes obtained from bovine brain cortex phospholipids affect benserazide-induced hyperprolactinemia. Benserazide induces an increase of serum prolactin in man, possibly by impairing the dopamine effect on the pituitary and/or the outer median eminence caused by inhibition of L-dopa decarboxylase. Liposomes obtained from bovine brain cortex phospholipids, however, reduce serum prolactin, possibly through an effect of phosphatidylserine on dopamine biosynthesis at the level of tyrosine hydroxylase. Oral doses of 125mg benserazide given to five normal Ss induced an increase of serum prolactin that did not change when 300mg of phospholipid liposomes were given intravenously 60 min. later. An increase of L-dopa synthesis apparently is not capable of overcoming the effects of decarboxylase inhibition. 11 references. (Author abstract modified)

002321 Needham, T. E.; Javid, P.; Brown, W. Baxter Travenol Laboratories, Morton Grove, IL **Bioavailability and dissolution parameters of seven lithium carbonate products.** *Journal of Pharmaceutical Sciences.* 68(8):952-954, 1979.

The bioavailabilities of seven commercial lithium carbonate products and a standard powder of lithium carbonate were examined following oral administration to healthy volunteers. An analysis of variance of saliva levels and urinary excretion showed no significant difference between the products, but sig-

nificant intersubject differences were found. A significant difference was found for the time of peak saliva levels, which was attributed to faster absorption of the powder. A dissolution study showed no significant difference between products after the lag time for the capsule dosage forms. 20 references. (Author abstract modified)

002322 Oyama, Tsutomu; Jin, Toshiro; Yamaya, Ryuji; Ling, Nicholas; Guillemain, Roger. Guillemain: Salk Institute, Laboratories for Neuroendocrinology, 10010 N. Torrey Pines Road, La Jolla, CA 92037 **Profound analgesic effects of beta-endorphin in man.** *Lancet.* No. 8160:122-124, 1980.

The analgesic effects of beta-endorphin were examined among 14 patients with chronic intractable pain secondary to metastatic malignancies. Profound and long lasting analgesia was produced by intrathecal administration of 3mg synthetic beta-endorphin in all the patients. The mean duration of pain relief was 33.4 hours, with a range from 22.5 hours to 73.5 hours. No respiratory depression, hypotension, hypothermia, or catatonia was observed. It is concluded that beta-endorphin which occurs naturally in the central nervous system is most likely involved in the normal physiological mechanisms of pain perception. 16 references. (Author abstract modified)

002323 Papavasiliou, Paul S.; McDowell, Fletcher H.; Rosal, Victoria; Miller, Samuel T. Dept. of Neurology, New York Hospital, 525 E. 68th St., New York, NY 10021 **Administration of human somatotropin in levodopa-treated patients with parkinsonism.** *Archives of Neurology.* 36(10):624-626, 1979.

To investigate further the role of growth hormone (GH) on the cerebral effects of levodopa, human somatotropin (human growth hormone) was administered to four patients with parkinsonism with varying response to chronic levodopa therapy. The doses of somatotropin (5IU) were administered on alternate days for 4 days, and the effects of this hormone on the patient's symptomatic control, dyskinesia, plasma GH, and dopa levels were evaluated and compared with those of patients receiving saline injections. Administration of exogenous human somatotropin, even during marked and sustained elevations of plasma GH levels did not alter the therapeutic or side-effects of levodopa therapy. With one exception, plasma dopa levels after human somatotropin administration remained unchanged. It is concluded that neither the endogenous increases of GH in response to levodopa nor those attained following human somatotropin administration modify in any consistent way the therapeutic effects and side-effects of chronic levodopa therapy, and that the episodic releases of GH in response to levodopa occur independently of its cerebral effects. 15 references. (Author abstract modified)

002324 Philipp, Michael; Beyer, J.; Happ, J.; Krause, U. Psychiatrische Universitätsklinik, Langenbeckstrasse 1, D-6500 Mainz, Germany **/Endocrinological prediction of the responsiveness of depressive patients to lofepramine./** *Endokrinologische Vorhersage der Therapieansprechbarkeit depressiver Patienten auf Lofepramin.* *Archiv für Psychiatrie und Nervenkrankheiten.* 227(1):71-79, 1979.

The hypothesis that neuroendocrinological parameters are apt to predict the thymoleptic efficacy of lofepramine was examined in a pilot study with 15 depressive patients of the neurotic and endogenous type. These parameters, which were measured with a simple global stimulation test (insulin hypoglycemia combined with injection of TRH and LHRH) were: high basal blood glucose, high hypoglycemic blood glucose, high decrease of blood glucose in comparison to the basal level, low basal TSH, low increase of HGH and low increase of cortisol after hypoglycemia. A synopsis of these parameters allowed a correction classifica-

tion of 14 out of 15 patients according to therapy response and therapy resistance. 29 references. (Author abstract)

002325 Post, Robert M. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Central stimulants: clinical and experimental evidence on tolerance and sensitization.** (Unpublished paper). Bethesda, MD, NIMH, 1979. 142 p.

Selected studies which provide evidence for tolerance and sensitization following chronic psychomotor stimulant administration are reviewed, and factors which may relate to the appearance of these apparently opposite responses are discussed. The factors associated with the development of behavioral sensitization and tolerance are examined: 1) altered blood levels; 2) dose and drug administration variables; 3) interval between drug administration; 4) behavioral, physiological, or biochemical end point measured; 5) subject populations studied (differences among populations depending upon species, genetic subtype, and age); 6) environmental context and conditioning factors in behavioral sensitization and tolerance; 7) endocrine and stress components of chronic responses to psychomotor stimulant administration; and 8) state-dependent and rate dependent effects of the psychomotor stimulants in relation to sensitization and tolerance. The postulated mechanism for behavioral sensitization to the psychomotor stimulants and related compounds includes: drug metabolism and disposition, increases in presynaptic catecholamine response, a denervation or depletion supersensitivity mechanism, possible increased postsynaptic receptor effects accounting for behavioral sensitization, presynaptic receptor desensitization and behavioral sensitization with relevance to temporal lobe epilepsy and alcohol withdrawal. The clinical implications of the development of tolerance and sensitization to the central stimulants include: 1) sensitization to paranoid psychoses; 2) sensitization to manic episodes; 3) sensitization to levo-dopa in Parkinsonism; and 3) sensitization or tolerance to repeated environmental stresses. 297 references.

002326 Richards, C. D. Dept. of Physiology, Royal Free Hospital School of Medicine, Pond Street, London NW3 2QG, England **In search of the mechanisms of anaesthesia.** *Trends in NeuroSciences*. 3(1):9-13, 1980.

The experimental literature on mechanisms mediating anaesthesia is reviewed, and sites of action, the cellular basis of anesthetic effects, and molecular mechanisms are discussed. Review of the present evidence on these topics suggest that there is no single mechanism by which all anesthetics produce their effects. It seems more likely that different anesthetics act at different sites to produce a number of lesions which are the basis of the anesthetic state. Anesthetics depress excitatory transmission by decreasing the amount of transmitter released from presynaptic terminals or by decreasing the sensitivity of the postsynaptic membrane to released transmitter, or by both effects together. A number of anesthetics appear to enhance inhibitory synaptic transmission. There is no sound evidence that anesthetics produce their characteristic behavioral effects by an action at a specific site in the brain, e.g., the ascending reticular formation. Rather it seems that anesthetics affect synaptic transmission throughout the brain, including the reticular formation, the thalamus, and the cortex. 15 references. (Author abstract modified)

002327 Riederer, P. Ludwig-Boltzmann-Institute of Clinical Neurobiology, Krankenhaus Lainz, Pavillon II, Wolkersbergstrasse 1, A-1130 Vienna, Austria **The distribution and metabolism of L-tryptophan in healthy probands under dietary conditions.** *International Journal of Clinical Pharmacology, Therapy and Toxicology*. 18(1):31-36, 1980.

The distribution and metabolism of L-tryptophan (TRP) in healthy probands under dietary conditions were investigated. Oral administration of 500mg or 1,500mg of TRP to healthy probands resulted in a significant increase in free and bound TRP in plasma 2 hours after consumption. Serotonin and 5-hydroxyindole-3-acetic acid (5-HIAA) also demonstrated a significant increase in plasma, while tyrosine shows no change. However, a competitive reciprocity exists between the uptake of tryptophan and tyrosine because TRP increased significantly in the platelets after administration, and tyrosine was reduced. The concentration of serotonin also decreased, an effect which also indicates a competitive reciprocity between tryptophan and serotonin uptake. Hence, the platelet may be employed as a (neuronal) model for the study of mechanisms of amino acid transport through membranes and the factors by which they are influenced. Studies on metabolites of biogenic amines in urine, that is, indole-3-acetic acid (IAA), 5-HIAA, homovanillic acid (HVA), and vanillylmandelic acid (VMA) showed significant increase in IAA, 5-HIAA, and HVA after administration of 1,500mg TRP. The increased concentration of HVA is traced to synthesis of serotonin in dopaminergic neurons, which leads to temporary secretion of dopamine, and subsequently, HVA. 35 references. (Author abstract modified)

002328 Ross, Svante B.; Aperia, Bo; Beck-Friis, Johan; Jansa, Sten; Wetterberg, Lennart; Aberg, Anna. Research and Development Laboratories, Astra Lakemedel AB, S-15185 Sodertalje, Sweden **Inhibition of 5-hydroxytryptamine uptake in human platelets by antidepressant agents in vivo.** *Psychopharmacology*. 67(1):1-7, 1980.

The accumulation of 14C-5-hydroxytryptamine (14C-5-HT) in platelet rich plasma (PRP) and the concentration of 5-hydroxytryptamine (5-HT) in whole blood of patients treated with the antidepressant agents zimelidine, desipramine, and clomipramine were examined before and during the treatment. Clomipramine and zimelidine markedly reduced the accumulation of 14C-5-HT and the concentration of 5-HT in the blood. Desipramine had a weaker, but significant effect. Added to the PRP in vitro clomipramine was 10 times more potent than norzimelidine, the active metabolite of zimelidine, and 60 and 300 times more active than desipramine and zimelidine, respectively in inhibiting the accumulation of 14C-5-HT. Analysis of plasma concentrations of zimelidine and norzimelidine showed that the decreased blood 5-HT and the inhibition of the 14C-5-HT accumulation in platelets was mainly produced by norzimelidine. The inhibition of the 14C-5-HT accumulation and the decrease in blood 5-HT by desipramine were significantly correlated to the log plasma concentration of desipramine. It is concluded that the decrease in blood 5-HT caused by these agents is due to the inhibition of 5-HT uptake in platelets. The half-life of the decrease in blood 5-HT after clomipramine and zimelidine was about 5 days. The return to normal 5-HT level after withdrawal of the drugs was 14 days or longer. These observations might indicate that only the newly formed platelets can accumulate 5-HT. 27 references. (Author abstract modified)

002329 Rotrosen, John; Angrist, Burton; Gershon, Samuel; Paquin, Jeanne; Branchey, Laura; Oleshansky, Marvin; Halpern, Frieda; Sachar, Edward J. Dept. of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016 **Neuroendocrine effects of apomorphine: characterization of response patterns and application to schizophrenia research.** *British Journal of Psychiatry*. 135(November):444-456, 1979.

Several studies were undertaken to further characterize apomorphine's stimulation of the release of growth hormone (hGH) and suppression of the release of prolactin (PRL) from the anterior pituitary. Studies in which apomorphine was given on two or three separate occasions to each of five Ss indicated that

the hGH response was a highly reproducible individual index, but PRL suppression was a less satisfactory measure. The hGH responses to apomorphine were consistently antagonized by pretreatment with haloperidol, supporting the concept that the hGH releasing effect of apomorphine is mediated by its action on dopamine receptors. Cyproheptadine pretreatment was associated with erratic increases or decreases in the hGH response to apomorphine, but did not alter PRL levels or apomorphine-induced PRL suppression. The relationship of these findings to biological hypotheses of schizophrenia and to neuroleptic-induced receptor changes is discussed. 57 references. (Author abstract modified)

002330 Ryall, Ronald W. Dept. of Pharmacology, University of Cambridge, Churchill College, Cambridge, England **Mechanisms of drug action on the nervous system.** Cambridge texts in the physiological sciences, vol. 1. New York, Cambridge University Press, 1979. 144 p. \$5.50.

The mechanisms by which drugs modify the operation of the nervous system, either to produce therapeutically useful effects or to cause undesirably toxic side-effects, are examined. Topics discussed include: pharmacology and anatomy of the neuromuscular junction, synaptic transmission, acetylcholine receptor activation, sites of drug action, pharmacology of the autonomic nervous system, ganglionic synapses, peripheral noradrenergic and cholinergic synapses, routes of drug administration, techniques used to study transmitters and drug action in the CNS, acetylcholine, amino acids, catecholamines, 5-hydroxytryptamine, polypeptides, types of general anaesthetic, mechanisms of anaesthesia, tolerance to anaesthesia, pharmacological control of pain, aspirin-like drugs, morphinelike drugs, drugs and disorders of movement, convulsants, antiepileptic agents, spasticity, Wilson's disease, Huntington's chorea, Parkinson's disease, anxiety reduction, muscle relaxant actions, sedatives, drugs used in schizophrenia, range and mechanisms of action, interaction with dopamine receptors, extrapyramidal side-effects, drugs used in psychotic depression, and psychotomimetic drugs. 83 references.

002331 Schachter, M.; Blackstock, J.; Dick, J. P. R.; George, R. J. D.; Marsden, C. D.; Parkes, J. D. University Dept. of Neurology, Institute of Psychiatry, London SE5, England **Liuride in Parkinson's disease.** *Lancet*. No. 8152:1129, 1979.

A clinical trial of liuride in the treatment of 11 patients with idiopathic Parkinson's disease is described. Parkinsonian symptoms and signs, tremor, rigidity, akinesia, and postural abnormality, as well as dyskinesia and other side effects, were assessed before liuride treatment and at 2, 4, and 8 weeks. Five patients taking liuride daily were withdrawn from the trial due to increase in akinesia and tremor, persistent nausea and visual hallucinations, and disorientation. It is concluded that liuride has definite antiparkinsonian action and may prove useful, since its dopamine agonist action appears to be independent of either dopamine synthesis or dopamine stores. 5 references.

002332 Shah, Nandkumar S.; Burch, Earl A.; Yates, Jane D.; May, Debbie A.; Donald, Alexander G.; Freed, Joe E.; Pressley, Lucius C. Ensor Foundation Research Laboratory, William S. Hall Psychiatric Institute, Columbia, SC 29202 **Dopamine uptake by human blood platelets.** *Research Communications in Psychology, Psychiatry and Behavior*. 5(1):25-35, 1980.

Dopamine uptake by human blood platelets was investigated. Platelet rich plasma was incubated with ¹⁴C-dopamine at either 37 degrees C or 4 degrees C, and dopamine uptake was measured. Platelets from human volunteers ranging in age from 18 to 40 years were found to accumulate equivalent amounts of dopamine. Pargyline caused a small but significant increase in platelet dopamine content. At 37 degrees C, chlorimipramine, am-

triptyline, and levo-methadone markedly reduced dopamine uptake. Low temperature was more effective than the 5-HT uptake inhibitors. Neuroleptic agents caused little inhibition. These results suggest that, at certain plasma concentration levels, circulating neuroleptics may not interfere with the in vitro uptake of dopamine by platelets. 17 references. (Author abstract modified)

002333 Sherwin, Duane. 14530 Sivertson Road N.E., Bainbridge Island, WA 98110 **A new method for treating American Journal of Psychiatry.** 136(9):1181-1183, 1979.

A 10 week study is described which was designed to gain some understanding of how to treat patients who have suffered for a long time with untreatable headaches. Fourteen patients, ranging in age from 20 to 50 years, had headaches at least 80% of waking time and were found to have depression according to the Zung depression scale. These patients were given varying amounts of perphenazine and amitriptyline with the direct suggestion that these drugs would be helpful. This treatment appeared successful for 10 of the 14 patients at 6 month and 3 year followup. 8 references. (Author abstract modified)

002334 Shore, D.; King, S. W.; Kaye, W.; Torrey, E. F.; Winfrey, H. J.; Potkin, S. G.; Weinberger, D. R.; Savory, J.; Wills, M. R. Laboratory of Clinical Psychopharmacology, Div. of Special Mental Health Research, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Serum and cerebrospinal fluid aluminum and circulating parathyroid hormone in primary degenerative (senile) dementia.** (Unpublished paper). Washington, DC, NIMH, 1980. 20 p.

Because previous CSF aluminum studies in primary degenerative (senile) dementia (PDD) patients have been contradictory and plagued with methodological problems, the CSF concentration of aluminum was measured by flameless atomic absorption spectrophotometry in patients controlled for age and hospitalization. The CSF aluminum concentrations were similar in PDD patients, neurological controls, and chronic schizophrenic patients matched for age. The results tend to confirm that the increases in CNS nuclear chromatin aluminum reported in PDD patients are not the result of a generalized overload of aluminum in biological fluids. It is suggested that further investigation of the interaction between aluminum and nuclear chromatin is warranted to determine whether aluminum is a factor in the etiology of neuronal degeneration in patients with PDD. 28 references.

002335 Smeraldi, E.; Scorza-Smeraldi, R.; Fabio, G.; Negri, F. Institute of Clinical Psychiatry, University of Milano, V. F. Sforza 35, I-20122 Milan, Italy **Interference between anti-HLA antibodies and CPZ metabolites.** *Psychopharmacology*. 67(1):87-89, 1980.

The interference of chlorpromazine (CPZ) and several preincubated CPZ metabolites on the lymphocyte absorption of antibodies directed against HLA-A1 and other nonrelated HLA specificities were investigated. Both CPZ and metabolites 7-OH-CPA, Norl-CPZ were found to interfere with the specific absorption of antiHLA-A1 antibodies. Implications are discussed. 11 references. (Author abstract modified)

002336 Stern, W. C.; Rogers, J.; Fang, V.; Meltzer, H. Burroughs Wellcome Co., Dept. of Clinical Research, 3030 Cornwallis Road, Research Triangle Park, NC 27709 **Influence of bupropion HCl (Wellbatrin), a novel antidepressant, on plasma levels of prolactin and growth hormone in man and rat.** *Life Sciences*. 25(20):1717-1724, 1979.

The effects of bupropion hydrochloride, a novel antidepressant, on plasma levels of prolactin (PRL) were determined in

normal human Ss and in male Sprague-Dawley rats. Single oral doses of 50, 100, or 200mg bupropion markedly suppressed (80% decrease) plasma PRL in male and female Ss, and PRL recovery was not complete within 24 hours. Small and erratic changes in plasma levels of growth hormone were also observed 1 to 4 hours after drug administration. In rats, single 25mg/kg i.p. doses of bupropion failed to lower basal PRL levels. However, bupropion significantly suppressed the elevation PRL induced by pretreatment with alpha-methyltyrosine, 5-hydroxytryptophan, or quipazine. Bupropion did not counteract the PRL elevating effect of haloperidol. Results suggest that bupropion has significant dopamine mimetic properties. 17 references. (Author abstract modified)

002337 Stone, Eric A. Millhauser Laboratories, Department of Psychiatry, New York University School of Medicine, New York, NY 10016 **Subsensitivity to norepinephrine as a link between adaptation to stress and antidepressant therapy: an hypothesis.** Research Communications in Psychology, Psychiatry and Behavior. 4(3):241-255, 1979.

The neurochemical and behavioral similarities in rats and humans between adaptation to chronic footshock stress and antidepressant therapy are reviewed and explained. The major points made from the review of neurochemical and behavioral similarities are: 1) both stress and antidepressants produce subsensitivity of norepinephrine (NE) in the rat brain; 2) adaptation to chronic stress in rats and chronic antidepressant therapy in humans are both accompanied by a loss of depressive symptoms; and 3) the respective time courses for the development of adaptation to stress, the clinical response to antidepressants and the appearance of subsensitivity to NE are similar, each requiring about 2 weeks. It is hypothesized that the development of subsensitivity of noradrenergic receptors facilitates the adaptation of emotional and physiological responses to chronic stress and in this manner decreases the ability of stress to induce depressive-like behavior. It is further proposed that antidepressant therapy is a unique form of adaptation to stress in which the various antidepressant treatments mimic the desensitizing actions of stress at noradrenergic receptors. The clinical action of these treatments may therefore result from a process similar to adaptation which increases resistance to stress. Methods of experimentally testing these hypotheses are discussed. 56 references. (Author abstract modified)

002338 Syvalahti, Erkkä; Eneroth, P.; Ross, S. B. Dept. of Psychiatry, University of Turku, SF-20700 Turku 70, Finland **Acute effects of zimelidine and alaproclate, two inhibitors of serotonin uptake, on neuroendocrine function.** Psychiatry Research. 1(2):111-120, 1979.

The accumulation of 145-5-hydroxytryptamine in human platelets in vitro and plasma levels of a number of hypophyseal hormones and cortisol in healthy male volunteers were determined after acute oral administration of zimelidine and alaproclate, two selective inhibitors of serotonin (5-HT) uptake. Alaproclate (100mg) significantly inhibited the accumulation of 14C-5-HT by 42% at 90 minutes but showed no significant effect at 4 hours. At 200mg the decrease in the accumulation was 55% after 90 minutes, and 31% after 4 hours. Zimelidine (200mg) caused a 72% decrease at 90 minutes, and 73% at 4 hours. Plasma levels of prolactin, growth hormone, luteinizing hormone, follicle stimulating hormone, and thyroid stimulating hormone remained unchanged after zimelidine and alaproclate; and the levels were comparable to those after placebo. A physiological decline of plasma cortisol levels was noted in the morning during the test period of 4 hours, but there were slight differences in the secretory pattern after the different drugs used. 22 references. (Author abstract)

002339 Tetsuo, Masahiro; Markey, Sanford P.; Colburn, Robert W.; Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Measurement of 6-hydroxymelatonin in human urine and its diurnal variations.** (Unpublished paper). Bethesda, MD, NIMH, 1980. 28 p.

Conjugated 6-hydroxymelatonin, the major urinary metabolite of the pineal hormone melatonin, was quantified using electron capture negative ion chemical ionization mass spectrometry. Human urine was hydrolyzed enzymatically and free 6-hydroxymelatonin extracted, reacted to form a stable t-butyldimethylsilyl-pentafluoropropionyl derivative which was separated on silica gel chromatography prior to gas chromatography mass spectrometry. In seven normal male subjects the mean daily urinary conjugated 6-hydroxymelatonin was 15.5micrograms (6.5 to 22.8micrograms). Urine samples at 6 hour intervals clearly demonstrated a 10 fold diurnal variation; from 0.8micrograms/6 hours during the day to 8.6micrograms/6 hours at night. 25 references. (Author abstract)

002340 Tormey, W. P.; Buckley, M. P.; Darragh, A. S. Department of Chemical Pathology, University of Leeds, Leeds General Infirmary, Leeds, LS1 3EX, England **Propranolol, sleep and the nocturnal release of stress hormones.** Irish Medical Journal. 72(10):450, 1979.

The effects of propranolol on the sleep related release of stress hormones at the dosage used in the treatment of anxiety were investigated. Six normal male volunteers aged 19 to 24 were studied in a sound attenuated laboratory for 14 nights. Propranolol (80mg) was ingested on nights 5 to 10, while placebos were administered on the other nights. The unaltered nocturnal secretion of ACTH, prolactin, and growth hormone suggests that propranolol did not reach the central catecholamine receptors involved in the release of these hormones. The main role of propranolol appears to be in the relief of peripheral adrenergic symptoms, although a central action has been shown by the use of very high doses in the treatment of schizophrenia (Yorkston et al., 1974). 8 references.

002341 Tune, Larry E.; Creese, Ian; DePaulo, J. Raymond; Slavney, Phillip R.; Coyle, Joseph T.; Snyder, Solomon H. Snyder: Dept. of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Clinical state and serum neuroleptic levels measured by radioreceptor assay in schizophrenia.** American Journal of Psychiatry. 137(2):187-190, 1980.

Serum neuroleptic levels were determined via radioreceptor assay in 30 schizophrenic patients receiving haloperidol, fluphenazine, chlorpromazine, molindone, thiothixene, or trifluoperazine. Neuroleptic levels were significantly correlated with clinical state, monitored by an abbreviated version of the Present State Examination (the mini-PSE). Poor therapeutic responses were associated with serum levels under 50ng/ml chlorpromazine equivalents. There was no correlation between neuroleptic dosage and mini-PSE score or between neuroleptic dose and serum neuroleptic levels. 21 references. (Author abstract modified)

002342 Uhde, Thomas W.; Redmond, D. Eugene, Jr.; Kleber, Herbert D. Redmond: 34 Park St., New Haven, CT 06508 **Clonidine suppresses the opioid abstinence syndrome without clonidine-withdrawal symptoms: a blind inpatient study.** Psychiatry Research. 2(1):37-47, 1980.

To investigate the effect of clonidine in the suppression of opioid withdrawal, nine hospitalized opioid addicted patients were blindly given clonidine within 36 hours of the abrupt and blind discontinuation of methadone. Results show that all patients were successfully withdrawn from methadone and were

asymptomatic upon discharge. Clonidine treated patients had significantly fewer symptoms than a comparable group of opioid addicts abruptly withdrawn from methadone. No exacerbation of symptomatology developed after the cessation of clonidine. Clinical implications of clonidine's suppression of opioid withdrawal, and the alpha 2 adrenergic mediation of the abstinence syndrome are discussed. 34 references. (Author abstract modified)

002343 Verebey, Karl; Blum, Kenneth. N.Y.A.S.A.S., 80 Hanson Place, Brooklyn, NY 11217 **Alcohol euphoria: possible mediation via endorphinergic mechanisms.** *Journal of Psychodetic Drugs.* 11(4):305-311, 1979.

The possibility of a common mechanism of action shared by psychoactive and euphorogenic substances is examined in order to elucidate a hypothetical mechanistic relationship between alcohol and opiate addiction. The published literature concerning the inner workings of the CNS is explored, with emphasis on opiate and alcohol related euphoria and its mediation by the endorphins. It is suggested that individual deficiencies in stress tolerance may be related to endorphin physiology; that the choice of drug used to cope with stress is influenced by external and internal forces; and that pleasure states induced by drugs are also attainable naturally via the endorphins. Further research in this regard may help eliminate substance abuse and provide free access to the beneficial use of euphorogens in therapeutic medicine and psychiatry. 63 references.

002344 Vlaar, H.; Bleeker, J. A. C.; Schalken, H. F. A. Bloemgracht 79, Amsterdam, Holland **Comparison between saliva and serum lithium concentrations in patients treated with lithium carbonate.** *Acta Psychiatrica Scandinavica.* 60(5):423-426, 1979.

The relation between serum and saliva lithium concentration was studied in patients treated with lithium carbonate. In 23 patients, a highly variable saliva/serum ratio was found in simultaneous saliva and serum samples. In five patients studied during a period of 4 to 8 weeks, three patients showed a high fluctuation in saliva/serum lithium ratio. In 20 patients, saliva lithium concentrations varied unexpectedly in a second sample produced after 15 minutes. It is concluded that the saliva lithium level is unreliable as a prediction of the serum lithium level in patients treated with lithium carbonate. 12 references. (Author abstract)

002345 White, Kerrin; Cohen, Jordan; Boyd, Jeffrey; Nelson, Richard. Dept. of Psychiatry, Los Angeles County - University of Southern California Medical Center, 1934 Hospital Place, Los Angeles, CA 90033 **Relationship between plasma, RBC, and CSF lithium concentrations in human subjects.** *International Pharmacopsychiatry.* 14(4):185-189, 1979.

Simultaneous measurements of plasma, red blood cell (RBC), and plasma lithium concentrations in 17 inpatients chronically treated with lithium were made at various times after the last lithium dose. RBC lithium levels were significantly higher than cerebrospinal fluid (CSF) lithium levels. Specimens drawn 10 or more hours after the last dose showed higher RBC and CSF lithium and lower plasma lithium than specimens drawn 4 or less hours after the last dose. None of the lithium measurements differentiated manic-depressives from schizophrenics or schizoaffectives. Plasma, RBC, and CSF lithium all intercorrelated highly and equally. 20 references. (Author abstract)

002346 Willer, Jean Claude; Bussel, Bernard. Laboratoire de Physiologie, Faculté de Médecine Saint-Antoine, 27 rue Chaligny, F-75571 Paris Cedex 12, France **Evidence for a direct spinal mechanism in morphine-induced inhibition of nociceptive reflexes in humans.** *Brain Research.* 187(1):212-215, 1980.

The direct spinal depressive action of morphine on nociceptive flexion reflexes and monosynaptic reflexes was examined in four chronic paraplegia spinal human volunteers. Polysynaptic nociceptive flexion reflexes (RII reflexes) of the lower limb were elicited by a supramaximal electrical stimulation of the ipsilateral sural nerve. Recordings were made on the tibialis anterior muscle (TA) using a couple of surface electrodes placed on the scratched and degreased skin above the muscle. Monosynaptic reflexes (H reflex) were elicited and recorded according to a classical method. Results confirm that morphine depresses selectively nociceptive spinal reflexes by a direct spinal mechanism in man. Moreover, this depressive effect is specific (since it is completely reversed by naloxone) and seems to play an important role in the modulation of nociceptive messages at spinal level (since usual therapeutic doses of the drug are able to exert a major depression on nociceptive flexion reflexes without affecting monosynaptic ones). 13 references.

002347 Yates, Celia M.; Loudon, J. B. MRC Brain Metabolism Unit, University Dept. of Pharmacology, 1 George Square, Edinburgh, EH8 9JZ, Scotland **Acetylcholinesterase status and inhibition of platelet monoamine oxidase following treatment with phenelzine.** *Psychological Medicine.* 9(4):777-779, 1979.

The activity of platelet monoamine oxidase (MAO) was measured in 22 severely depressed patients before and after treatment with 45mg and 60mg phenelzine. Results show that while acetylcholinesterase status may influence the degree of MAO inhibition during the first 2 weeks of phenelzine therapy, it would not appear to be related to MAO inhibition when treatment is continued for longer than 2 weeks. 8 references.

14 MECHANISM OF ACTION: BIOCHEMICAL

002348 Adam, Kirstine; Oswald, I. University Dept. of Psychiatry, Morningside Park, Edinburgh EH10 5HF, England **One gram of L-tryptophan fails to alter the time taken to fall asleep.** *Neuropharmacology.* 18(12):1025-1027, 1979.

The effects of 1g L-tryptophan and placebo on sleep latency were compared in 12 Ss who reported difficulty in falling asleep. The Ss also systematically varied the carbohydrate content of their evening meal, since diet can alter the uptake of tryptophan into the brain. No differences in sleep latencies were observed across any of the experimental conditions. Results fail to support the contention that 1g tryptophan may be of clinical use in treating sleep onset insomnia. 4 references.

002349 Anderson, J. A. D.; Dalton, E. R.; Basker, M. A. Department of Community Medicine, Guy's Hospital Medical School, London SE1 9RT, England **Insomnia and hypnotherapy.** *Journal of the Royal Society of Medicine.* 72(10):734-739, 1979.

The effectiveness of autohypnosis, nitrazepam, and placebo in the treatment of insomnia in general medical practice was evaluated in 18 patients. During weeks 1 through 4, patients received nitrazepam/placebo or placebo/nitrazepam. During weeks 5 to 8 patients continued with nitrazepam or placebo and were taught autohypnosis, which they continued through week 10, by which time all tablets had been withdrawn. Both patient and physician were blind to the nature of the tablets being taken. With respect to waking state, no significant differences were found among the three treatments. Patients slept significantly longer when on hypnosis alone than when on placebo. Significantly more patients had a normal night's sleep on autohypnosis alone than with placebo or nitrazepam. There was also a tendency for autohypnosis to reduce the time taken to go to sleep. Further research with a larger sample is recommended. 11 references. (Author abstract modified)

002350 Bixler, Edward O.; Scharf, Martin B.; Soldatos, Constantine R.; Mitsky, David J.; Kales, Anthony. Sleep Research and Treatment Center, Pennsylvania State University College of Medicine, Hershey, PA 17033 **Effects of hypnotic drugs on memory.** *Life Sciences*. 25(16):1379-1388, 1979.

Morning recall was assessed in 12 volunteer Ss given oral flunitrazepam (2mg) or secobarbital (100mg) at bedtime the night before. Both hypnotic drugs produced anterograde amnesia on the morning following the first drug night. This effect was still evident on the third drug night with flunitrazepam, but did not appear to be related to plasma drug concentrations. Results suggest that ingestion of certain benzodiazepine hypnotics at night may result in impaired retrieval of information acquired before sleep onset or during nocturnal awakenings. 27 references. (Author abstract modified)

002351 Cazzullo, Carlo L.; Sacchetti, E.; Smeraldi, E. Istituto di Clinica Psichiatrica—Guardia II, Via F. Sforza, 35, I-20122 Milan, Italy **Psychotropic drugs and their relationship with psychopathology and affective disorders.** *Progress in Neuro-Psychopharmacology*. 3(1-3):25-38, 1979.

The relationship between the psychopathology of depressive behavior and the effectiveness of drugs affecting mood is reviewed, and the following topics are discussed: nonpsychological validation of diagnosis of primary affective disorders, predictability of the response to antidepressant drugs, and factors involved in the effectiveness of long-term lithium treatment. It is hypothesized that the variability of the behavioral effects of psychotropic drugs may arise either from interindividual pharmacokinetic differences or from at least three other factors: 1) inefficiency of currently used diagnostic categories for distinguishing between different diseases which closely resemble each other, 2) existence of multiple biochemical mechanisms underlying a single disorder, and 3) problems related to the psychosocial environment (e. g., differences in the attitudes and expectations of the patient about the drug treatment associated with differences in the psychodynamics of the individual and the doctor/patient relationship. 33 references. (Author abstract modified)

002352 Chiarenza, Giuseppe A.; Rho, Marco; Resele, Leonardo. Istituto di Neuropsichiatria Infantile, Via G. Besta 1, I-20161 Milano-Affori, Italy **The hangover effects of some benzodiazepines studied by means of the contingent negative variation (C.N.V.) and neuropsychological tests.** *Research Communications in Psychology, Psychiatry and Behavior*. 4(4):371-382, 1979.

The hangover effects of three benzodiazepines: chlordesmethyldiazepam, desmethyldiazepam, and diazepam were compared with a placebo, using the Contingent Negative Variation and a series of neuropsychological tests. The results show that 8 hours after the administration of the drugs, no remarkable modifications of the Contingent Negative Variation can be detected. The neuropsychological tests show instead a clearly negative effect of chlordesmethyldiazepam on those performances which involve more complex cognitive functions. The clinical use of chlordesmethyldiazepam is suggested as more practical than that of other benzodiazepines. 18 references. (Author abstract modified)

002353 Cianchetti, Carlo; Masala, Carmelo; Mangoni, Alfonso; Gessa, Gian Luigi. Institute of Neurology, University of Cagliari, Cagliari, Italy **Suppression of REM and delta sleep by apomorphine in man: A dopamine mimetic effect.** *Psychopharmacology*. 67(1):61-65, 1980.

The suppression of REM and delta sleep by apomorphine in man was investigated. Apomorphine, a direct stimulant of dopamine receptors, was given in nonemetic doses by continuous IV infusion of 180 to 240 minutes during night sleep in normal

human Ss. During apomorphine infusion, a significant reduction of stage (S)4 and an abolition of REM sleep occurred. The percent duration of S2 was significantly increased. In the 240 minutes following interruption of a 240 minute infusion of apomorphine, a significant increase of S4 and REM percent duration was observed. The effect of apomorphine infusion on sleep was prevented by the administration of haloperidol or sulpiride, two dopamine receptor blocking agents. This suggests that this effect is due to a dopamine mimetic action. 28 references. (Author abstract modified)

002354 Coyle, Joseph T. Dept. of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD 21305 **Pharmacotherapy for anxiety.** *Psychiatric Annals*. 9(10):10-15, 1979.

The use of psychotropic medications to treat symptoms of anxiety in several psychiatric disorders is reviewed. It is suggested that when anxiety is secondary to an underlying condition such as an affective disorder or schizophrenia, drug treatment of the primary disorder should be instituted before symptomatic treatment of the anxiety. In the case where anxiety is a primary symptom, such as in agoraphobia or anxiety neurosis, tricyclic antidepressants, phenelzine, and possibly beta-receptor blockers can be effective in reducing somatic concomitants of anxiety; for the psychic tension and anticipatory anxiety, benzodiazepines tend to be more effective. In atypical depression with anxiety, phenelzine appears to be the drug of choice. It is suggested that the use of benzodiazepines in the treatment of character disorders with chronic high levels of anxiety should be approached with caution. 7 references.

002355 Davis, G. C.; Buchsbaum, M. S.; Bunney, W. E., Jr. Biological Psychiatry Branch, Building 10, Room 2N210, 9000 Rockville Pike, Bethesda, MD 20205 **Pain and psychiatric illness.** (Unpublished paper). Bethesda, MD, NIMH, 1979. 17 p.

In an examination of pain and psychiatric illness, 17 off medication hospitalized schizophrenics and 17 age matched and sex matched normal controls were tested for pain sensitivity. Schizophrenics were, on the average, less pain sensitive than controls. Also, the chronic effect of naltrexone was tested in five schizophrenic patients: the increase in pain sensitivity was striking. Studies of pain appreciation in affective illness are reviewed, and it is shown that, while both affective illness patients and schizophrenics are less sensitive to experimental pain, affectively ill patients report more somatic distress. As with schizophrenics, there is indirect and preliminary evidence suggesting that endorphins may play a role in both the depressive mood and pain insensitivity of affective illness. The effects of psychotropic drugs in the perception of pain are examined, and psychogenic pain is discussed. 54 references.

002356 Davis, Kenneth L.; Mohs, Richard C.; Tinklenberg, Jared R.; Hollister, Leo E.; Pfefferbaum, Adolf; Kopell, Bert S. Bronx Veterans Administration Hospital, Psychiatry Service (A223), 130 Kingsbridge Rd., Bronx, NY 10468 **Cholinomimetics and memory: the effect of choline chloride.** *Archives of Neurology*. 37(1):49-52, 1980.

The effect of choline on a group of normal young Ss who previously participated in a trial of physostigmine was studied. Ss received 16g of choline chloride in a double-blind A-B-A design. Short-term and long-term memory function was evaluated. Comparison of group means indicates that choline chloride did not significantly affect short-term memory or long-term memory. However, individual Ss may have had some aspects of long-term memory affected by choline chloride treatments. The results suggest that the effect of lower doses of choline on long-term memory should be evaluated. 58 references. (Author abstract modified)

002357 DeVeau-Geiss, Joseph; Joseph, Anthony. 750 East Adams Street, Syracuse, NY 13210 **Paradoxical response to amphetamine in a hyperkinetic adult.** *Psychosomatics*. 21(3):247, 251-252, 1980.

The case of a man with hyperkinetic syndrome is reported emphasizing his responses to a stimulant drug, dextroamphetamine sulfate. In response to dextroamphetamine, the patient displayed reduction of anxiety and motor activity, increased concentration, depression of mood, drowsiness, reduction of aggressive impulses, and the disappearance of paranoid ideation. The finding supported the interpretation that the paradoxical behavioral response to amphetamine may have represented a truly paradoxical response, in the pharmacological sense, of the central nervous system to a stimulant drug. 16 references.

002358 Duriez, R.; Barthelemy, Cl.; Rives, H.; Courjaret, J.; Gregoire, J. Rhone-Poulenc - Spécia, Direction des Recherches Thérapeutiques, 16, rue Clisson, F-75646 Paris Cedex 13, France **Treatment of sleep problems using zopiclone: double-blind cross-over clinical trials.** *Traitement des troubles du sommeil par la zopiclone: essais cliniques en double insu contre placebo.* *Thérapie*. 34(3):317-325, 1979.

The use of zopiclone, a compound with similar properties to the benzodiazepines, in treating outpatient insomnia was investigated. A cross-over double-blind design was used for two consecutive periods of 7 days and three doses of zopiclone (5, 7.5, and 10mg in a single evening dose) were used. The drug proved effective in treating the sleep disturbances at all three dosages, with efficacy increasing with higher doses. 8 references. (Author abstract modified)

002359 Evans, Ian M.; Distiller, Larry A. Dept. of Psychology, University of Hawaii, Honolulu, Hawaii **Effects of luteinizing hormone-releasing hormone on sexual arousal in normal men.** *Archives of Sexual Behavior*. 8(5):385-395, 1979.

To investigate the influence of luteinizing hormone releasing hormone (LRH) on libido and potency in human males, six normal adult male subjects were administered either LRH or a saline placebo 10 minutes before a 40 minute laboratory session in which they were exposed to erotic stimuli. Subjects attended four such sessions, twice receiving LRH and twice the placebo in a balanced, double-blind, crossover design. Rapidity of onset of erection, maximum degree of erection obtained, and overall levels of tumescence were consistently greater following LRH administration; however, the differences were not statistically significant. Luteinizing hormone and follicle stimulating hormone response to LRH was noted; no significant alteration in serum testosterone was observed. It is concluded that further investigation of the behavioral effects of LRH appears justified. 14 references. (Author abstract modified)

002360 Fleiss, Joseph L. Division of Biostatistics, Columbia University, New York, NY **Subject-own-control designs from a statistical perspective.** *Psychopharmacology Bulletin*. 15(3):42-44, 1979.

Problems in the use of the subject-own-control designs in evaluating the effects of psychotropic drugs are discussed. The planning and analysis of these designs has improved since Chasman first proposed them; for example, most now incorporate some sort of randomization scheme for the determination of drug order. The major advantage asserted for the intensive designs is their ability to reveal subtypes within an apparently homogeneous group of patients. However, interpatient variability in drug response has been observed for every agent currently available, and this variation is not necessarily associated with discrete typological differences. 8 references.

002361 Hach, B.; Hartung, M.-L. Universitäts-Nervenklinik mit Poliklinik im Kopfklinikum, Schwabachanlage 6 und 10, D-8520 Erlangen, Germany **The effect of penicillamine on the psychopathological disorders related to hepatocerebral degeneration (Wilson's disease).** *Die Wirkung des Penicillamins auf die psychopathologischen Veränderungen der hepatocerebralen Degeneration.* *Nervenz. 50(2):115-120, 1979.*

The effect of penicillamine on psychopathological disorders accompanying hepatocerebral degeneration (Wilson's disease) is described. Five patients were studied, who were given the drug orally in doses of 900 to 1,800mg/day. There was no additional psychiatric therapy. The mental condition of the patients was checked after 5 to 7 months of treatment. Clinical, psychopathometric, and psychological tests were evaluated. In four out of five cases, the accompanying syndrome disappeared after 5 to 7 months. Only in one case did it take 7 months before the clinical picture of the patient improved. It was found that the psychopathological disorders of the hepatocerebral degeneration did not result in irreversible damage (dementia), but in a reduced function of the brain, which could be restored (passing syndrome). It was found that increased elimination of copper by penicillamine and reduced intake of copper by potassium sulfide and low copper diet can stop the inherent advance of hepatocerebral degeneration and actually improve the clinical disorders. This applies also to mental disorders. 19 references. (Author abstract modified)

002362 Hartmann, Ernest; Spinweber, Cheryl L. Boston State Hospital, Boston, MA 02124 **Sleep induced by L-tryptophan: effect of dosages within the normal dietary intake.** *Journal of Nervous and Mental Disease*. 167(8):497-499, 1979.

Further experiments extending previous results which have demonstrated sleep inducing effects of L-tryptophan in doses of 1 to 15g at bedtime are presented. The present laboratory study extends the dose response curve downward, comparing doses of .25g, .50g, and 1g of L-tryptophan with placebo, in 15 mild insomniacs (subjects who reported sleep latencies of over 30 minutes). One gram of L-tryptophan significantly reduced sleep latency: the lower doses produced a trend in the same direction. Stage IV sleep was significantly increased by .25g of L-tryptophan. These results at low doses have noteworthy implications since the normal dietary intake of L-tryptophan is .50g to 2g per day. 21 references. (Author abstract modified)

002363 Herold, Edward; Mottin, James; Sabry, Zak. Dept. of Family Studies, University of Guelph, Guelph, Ontario, Canada N1G 2W1 **Effect of vitamin E on human sexual functioning.** *Archives of Sexual Behavior*. 8(5):397-403, 1979.

To investigate the claim that vitamin E can affect human sexual functioning, 1000 IU vitamin E, alpha tocopherol, were administered daily for 28 days in a double-blind placebo study. Thirty-five subjects in this pilot study reported daily responses to questionnaires on sexual arousal and behavior. No differences in sexual arousal or behavior were found between the two groups. The one significant difference was that the vitamin E subjects were more likely than the placebo subjects to report either positive or negative nonsexual effects. Directions for future research are suggested. 11 references. (Author abstract modified)

002364 Horita, Hideki; Hoashi, Eiichi; Okuyama, Yuko; Kumagai, Koumei; Endo, Shiro. Dept. of Pediatrics, Jikei University School of Medicine, Tokyo, Japan **Overnight polygraphic studies of infantile spasms -- influence of hormone therapy on sleep states, pulse, respiration and seizure activities.** *Folia Psychiatrica et Neurologica Japonica*. 33(3):269-277, 1979.

The effects of ACTH and hydrocortisone on sleep states, pulse, respiration, and seizure activities in four cases of infantile spasms were examined by means of overnight sleep polygraphy, and the effects of these drugs on these parameters were compared between those cases with good prognosis and those cases of poor prognosis. In all cases, the awake time in bed during hormone therapy was longer than before hormone therapy. The reduction of REM sleep time and lowering of REM density were remarkable during hormone therapy in cases with delayed psychomotor development as compared with cases with a considerable degree of psychomotor development. During hormone therapy, the pulse rate increased significantly in cases with considerable degree of psychomotor development, but decreased significantly in cases with delayed psychomotor development. In cases with hypsarhythmic EEG records, the number of spikes decreased drastically with hormone therapy, while in cases with EEG record of focal spikes, the number of spikes increased. 23 references. (Author abstract modified)

002365 Jeste, Dilip V.; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, Division of Special Mental Health Research, NIMH, Washington, DC **Guidelines for the use of neuroleptics in clinical practice.** *Psychiatric Annals.* 10(1):39, 43-47, 51-52, 1980.

Suggestions for the prevention of tardive dyskinesia in (TD) psychiatric patients and for management of the condition when it does occur are presented. When the diagnosis is other than schizophrenia, management without neuroleptics should be considered. In treatment of schizophrenia, risks of long-term treatment with neuroleptics should be discussed with the patient and his family and the continuing need for neuroleptics should be assessed and documented. When TD is suspected or diagnosed, a sequential procedure of management is recommended which includes diagnosis, informing the patient and family, trial of neuroleptic withdrawal, and discontinuation of antiparkinsonian drugs. Circumstances under which continuation of neuroleptic therapy, despite TD, is desirable are listed, and guidelines for continuation of neuroleptics in such patients are provided. 7 references.

002366 Kolakowska, Tamara; Orr, Michael; Gelder, Michael; Heggie, Manuela; Wiles, David; Franklin, Michael. University of Oxford, Dept. of Psychiatry, Littlemore Hospital Research Unit, Oxford OX4 4XN, England **Clinical significance of plasma drug and prolactin levels during acute chlorpromazine treatment: a replication study.** *British Journal of Psychiatry.* 135(October):352-359, 1979.

The plasma levels of the drug, plasma prolactin (PRL), side-effects, and changes in mental state of psychotic patients receiving chlorpromazine (CPZ) treatment were examined with 19 patients in a replication study. The results confirm some of the earlier findings: plasma CPA levels vary widely among patients and correlate poorly with daily doses of CPZ, increased plasma PRL is associated with higher plasma CPZ levels and is more common among the patients who develop side-effects, and none of these three variables differ between groups of patients with good and poor treatment outcome. It is concluded that previous findings of a significant association between side-effects and higher plasma CPZ were not confirmed. 24 references. (Author abstract modified)

002367 Kyriakides, Mary; Silverstone, T. Medical College of St. Bartholomew's Hospital, German Hospital, Ritson Road, London E8 1DF, England **Comparison of the effects of d-amphetamine and fenfluramine on hunger and food intake in man.** *Neuropharmacology.* 18(12):1007-1008, 1979.

The effects of fenfluramine (FF, 40, 60, and 80mg), d-amphetamine (d-AMP, 10mg), and placebo on hunger and food intake were studied in healthy female volunteers. The 80mg FF dose was about as potent as 10mg d-AMP in subjective anorectic effect, but caused a much greater suppression of food intake. The 60mg FF dose was equipotent to 10mg d-AMP in suppression of food intake, but was far less potent in reducing hunger ratings. These differences in relative potencies may reflect the different neuropharmacological actions of the two drugs. In contrast to findings in rats, no difference in the pattern of food intake produced by 60mg FF and 10mg d-AMP was found; both drugs led to an increase in the latency to eat and a decrease in the rate of feeding. 8 references.

002368 Liljequist, R.; Palva, E.; Linnoila, M. Siltavuorenpenger 10 A, SF-00170 Helsinki 17, Finland **Effects on learning and memory of 2-week treatments with chlordiazepoxide lactam, N-desmethyldiazepam, oxazepam and methyloxazepam, alone or in combination with alcohol.** *International Pharmacopsychiatry.* 14(4):190-198, 1979.

The effects of a 2-week treatment with chlordiazepoxide lactam (5mg), nordiazepam (10mg), oxazepam (15mg) and methyloxazepam (20mg) on immediate memory and associative learning were investigated in 40 healthy students. Oxazepam and methyloxazepam alone behaved similar to a placebo drink. Immediate memory was significantly impaired following treatment with nordiazepam, chlordiazepoxide lactam, alcohol, and after the simultaneous administration of nordiazepam and chlordiazepoxide lactam with alcohol. Chlordiazepoxide lactam was the only drug which alone impaired associative learning. Alcohol alone and all drugs in combination with alcohol retarded learning acquisition. 25 references. (Author abstract modified)

002369 Lonowski, Daniel J.; Sterling, F. E.; King, Hugh A. PO Box 31, Pineville, LA 71360 **Electromyographic assessment of dimethylaminoethanol (deanol) in treatment of tardive dyskinesia.** *Psychological Reports.* 45(2):415-419, 1979.

An ABAB reversal design with matched placebo was employed to assess the acetylcholine precursor, dimethylaminoethanol (deanol) in the treatment of tardive dyskinesia in two male and two female chronic schizophrenics. Oral dyskinesia was monitored by EMG, and a battery of psychological rating scales was also used to determine effects of deanol on psychological functioning. Improvement ranged from 35% to 70% dyskinetic symptom reduction in three patients given deanol. The decrease in symptomatology, however, did not reach the level of oral EMG activity observed in a normal control subject. Psychological functioning was generally unaffected, but slight improvement was seen in two subjects. 10 references. (Author abstract modified)

002370 Lycaki, Helene; Josef, Norma C.; Munetz, Mark. Josef: Adult Inpatient Service, Lafayette Clinic, 951 East Lafayette, Detroit, MI 48207 **Stimulation and arousal in self-mutilators.** *American Journal of Psychiatry.* 136(9):1223-1224, 1979.

The effects of a stimulant medication, methylphenidate, on the behavior of two patients with a history of self-mutilation were examined. The immediate results of the therapeutic trial were dramatic. The response of these two patients supports the theory that self-mutilators may have a deficit in their arousal systems that interferes with a transmittal to appropriate centers. This in turn results in the need to engage in mutilating behavior to provide adequate stimulation. It is concluded that this is only a theoretical consideration and needs to be tested in controlled research. 4 references.

002371 Mattes, Jeffrey. Long Island Jewish-Hillside Medical Center, Long Island, NY **The effect of food coloring on chil-**

dren's behavior. (Unpublished paper). Final Report, NIMH Grant R03-MH-32025, 1979. 5 p.

Hyperactive children (eight boys and five girls) participated in a study of the effects of food coloring on their behavior. The study was designed to maximize the likelihood of detecting an effect of the artificial food colorings. Only children who were maintained on the diet with supposedly markedly beneficial effect and who were reported to be very adversely affected by dietary violations were tested. No support for the contention that artificial food coloring affects deleteriously the behavior of preselected children was obtained. It is suggested that the hyperactive symptomatology is very strong.

002372 McPartland, Richard J.; Kupfer, David J.; Coble, Patricia; Shaw, David H.; Spiker, Duane G. Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA **An automated analysis of REM sleep in primary depression.** Biological Psychiatry. 14(5):767-776, 1979.

The REM sleep of 23 nonpsychotic patients with primary depression was studied by means of an automated REM analyzer during a drug free period and again during amitriptyline administration. Initial drug administration (50mg) was associated with an immediate reduction in the number, average frequency, and average size of the rapid eye movements. The average REM size remained suppressed with continued drug administration while the average REM frequency showed a rebound which was responsible for a partial recovery of the number of REMs and total REM intensity to predrug levels. With regard to individual REM periods, REM frequency and REM intensity were redistributed during tricyclic administration so that the second REM period became more analysis technique is seen as providing an objective set of measures for characterizing discrete aspects of REM sleep during a depressive episode and for evaluating the changes in REM sleep during psychotropic trials. 14 references. (Author abstract)

002373 Mendelson, Wallace B.; Goodwin, Donald W.; Hill, Shirley Y.; Reichman, John D. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Interaction of benzodiazepine hypnotics and ethanol.** (Unpublished paper). Washington, DC, NIMH, 1979. 1 p.

The literature on the interaction of benzodiazepine hypnotics and ethanol was reviewed, and an electroencephalograph (EEG) study of the interaction of ethanol with the hypnotics flurazepam and triazolam was conducted. Young adult male volunteers (47) had baseline clinical waking EEGs at 3:30 p.m. on the day of the study; at 5:00 p.m. they were given either 30mg flurazepam, 0.25mg triazolam, or placebo. Fifty minutes later, a second EEG was performed, and the subjects were given ethanol (0.8mg/kg) or ethanol placebo. Fifty minutes afterwards a third EEG was performed; subjects went to bed and the following morning a fourth EEG was done, 16 hours after the original medication. The presence of a drug effect was determined visually by criteria drawn from the literature and validated by blind readings of the second EEG. Analysis of the fourth EEG found no effect due to either triazolam alone or triazolam plus ethanol. In contrast, drug effects were present in 86% of the records of those who had taken flurazepam plus ethanol. (Author abstract modified)

002374 Michalska, Irena. Ośrodek Naukowo-Dydaktycznego AM, Oddział Neurologiczny, Grenadierów 51/59, 04-073 Warsaw, Poland /**Evaluation of the effects of anginin in cerebrovascular diseases in the light of psychological investigations.**/ Ocena działania angininy w chorobach naczyń mózgu w

świetle badań psychologicznych. Neurologia I Neurochirurgia Polska. 13/29(2):141-146, 1979.

Seventeen patients aged 40 to 69 years with cerebral atherosclerosis and peripheral atherosclerotic changes treated for 6 months with anginin were investigated psychologically to assess the effects and the influence of patients' attitudes on health improvement. Each patient was investigated psychologically to assess the effects of the drug on higher psychic functions and motor fitness, duration of drug effects, and the influence of patients' attitudes on health improvement. Each patient was investigated four times using a set of psychometric tests and interviews, before starting treatment, after 3 to 4 months of treatment, 6 months after beginning treatment, and 6 months after completion of treatment. Seven patients received placebo for the first 2 months. Results indicated that during treatment immediate and delayed visual and auditory memory increased, visuo-motor coordination improved, and disturbances of attention, concentration, and motor fitness were alleviated. These results improved further after 3 to 4 months of treatment. The effect of anginin lasted for 6 months after completion of treatment. A strong influence of the attitude of patient on health improvement is reported. 6 references. (Journal abstract modified)

002375 Mohs, Richard C.; Davis, Kenneth L. Psychiatry Service (116A), VA Medical Center, 130 W. Kingsbridge Rd., Bronx, NY 10468 **Choline chloride effects on memory: correlation with the effects of physostigmine.** Psychiatry Research. 2(2):149-156, 1980.

To explore dose response characteristics and individual differences in the cognitive effect of choline, choline chloride and placebo were administered to nine young adults in a placebo/drug/placebo design. Subjects took memory tests at the end of both placebo periods and at the end of the choline period. All nine subjects had participated in a previous study in which 1.0mg of physostigmine infused over a 1 hour period improved memory performance relative to performance during saline infusion. Choline had no significant effect on average performance either on a test of memory storage or on a test of memory retrieval. However, correlational analysis indicated that subjects who improved most when given physostigmine tended to show slight improvement when given choline. Results suggest that choline does not have substantial effects on memory but that there are small cognitive effects of choline in some subjects. 28 references. (Author abstract modified)

002376 Nasrallah, Henry A.; Holley, Thomas; Janowsky, David S. Dept. of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093 **Opiate antagonism fails to reverse hypnotic-induced analgesia.** Lancet. No. 8130:1355, 1979.

The failure of a high dose of naloxone to reduce or abolish hypnotic analgesia is discussed. A 22-year-old male volunteer who was susceptible to hypnosis was hypnotized and glove analgesia was introduced to his left hand. An intravenous injection of either 20ml of physiological saline or naloxone 50mg in 20ml of water was given over a 10 minute period before the measurement of pain perception. The results indicate that naloxone does not antagonize hypnotic-induced analgesia, suggesting that enorphins are probably not involved in this type of analgesia. The mechanism of hypnotic induced analgesia remains unknown and may involve an entirely different psychophysiological or neurological mechanism.

002377 Rothenberg, S.; Schottenfeld, S.; Gross, K.; Selkoe, D. Alcohol and Drug Abuse Research Center, McLean Hospital, Belmont, MA 02178 **Specific oculomotor deficit after acute meth-**

adone. I. Saccadic eye movements. *Psychopharmacology*. 67(3):221-227, 1980.

Changes in saccadic eye movements before and after up to 10mg oral methadone were measured electrooculographically in nontolerant nondependent humans. Undershoot of initial saccades increased with increasing size of horizontal target displacement (to 36 degrees) from a central viewing position. Dosage as low as 5mg caused significant increase in saccade undershoot, especially to target displacements greater than 10 to 15 degrees. Latency from target displacement to onset of initial saccade also increased after methadone. These results, in combination with the lack of significant drug effect on latency between initial saccade duration, maximum velocity, and time to maximum velocity indicate methadone action on specific sensory, rather than motor, components of saccadic response. The similarity of alteration of saccadic response after methadone and after lesion of the upper layers of the superior colliculus in primates, as reported in the literature, suggests that opiate binding sites in the upper layers of the superior colliculus may be physiologically active. 29 references. (Author abstract)

002378 Samet, Charles M.; Geller, Robert D. State University of New York, Stony Brook, NY 11790 **Anxiety associated with cardiovascular disorders: a study using lorazepam**. *Psychosomatics*. 20(10):709-713, 1979.

In a 4 week, double-blind study, lorazepam or placebo was given to 66 ambulant patients who suffered from anxiety associated with one of various cardiovascular disorders. Patients receiving lorazepam showed a significantly greater reduction of anxiety and related symptoms than did patients receiving placebo. Lorazepam was well tolerated in the dosages used and was compatible with other medications that were taken by the patients. 21 references. (Author abstract)

002379 Schain, Richard. University of California, Los Angeles, CA 90024 **Attentional behavior and drugs in hyperactive children**. (Unpublished paper). Final Report, NIMH Grant R01-MH-25076, 1979. 8 p.

Children 6 to 10 years old with symptoms of hyperactivity were the subjects in an investigation of attentional problems of hyperactive children. The clinical utility of tests of attentional behavior in identifying specific attention deficits of hyperactive children was investigated, and their value in monitoring the response to stimulation medication was assessed. Also, the value of low dose levels of methylphenidate was investigated. The findings support, in part, the theory that hyperactive children are subject to more rapid deterioration of the ability to sustain attention than normal children, and that stimulants improve this ability. However, the primary attentional problem manifested was poorer initial attention, rather than poorer ability to sustain attention. The Children's Checking Task appears to be a useful clinical tool for the diagnosis of attentional problems and for monitoring the effects of stimulants on attentional performance. Significant improvement was reflected on all attention measures at the 0.4mg/kg dosage of methylphenidate for those children who had poor initial performance on the Children's Checking Task.

002380 Smith, C. M.; Swash, M. Department of Pharmacology, London Hospital Medical College, Turner Street, London E1 2AD, England **Possible biochemical basis of memory disorder in Alzheimer's disease**. *Age and Ageing*. 8(4):289-293, 1979.

The effects of the anticholinesterase drug physostigmine on memory in a patient with familial Alzheimer's disease are reported. Physostigmine was chosen because it readily crosses the blood-brain barrier and is known to improve the short-term memory defect which occurs after overdosage with anticholin-

ergic drugs. The patient was a 42-year-old man, whose mother and uncle died of dementia before the age of 55. Progressive memory loss and personality change had occurred during the previous 2 years and on examination he was moderately demented. Testing was started 15 minutes after the injection, and was completed within an hour. A nonverbal test of intellectual capacity, Raven's Progressive Coloured Matrices (1965) and memory tests were used. Verbal memory was found to be poor and the patient made many intrusion errors. Physostigmine did not increase the amount of information remembered but reduced these intrusion errors. The reduction in intrusion errors is consistent with the suggestion that the memory defect in Alzheimer's disease is associated with damage to central cholinergic pathways. It is suggested that in Alzheimer's disease, as in Parkinson's disease, it is likely that patients will benefit more from pharmacological treatment in the early stages of the disease. 22 references.

002381 Smith, Gregory J.; Spear, Linda Patia; Spear, Norman E. Spear: Dept. of Psychology, State University of New York, Binghamton, NY 13901 **Ontogeny of cholinergic mediation of behaviors in the rat**. *Journal of Comparative and Physiological Psychology*. 93(4):636-647, 1979.

In a series of six experiments, cholinergic mediation of behavior was studied in immature rats. It was found that although scopolamine disrupted discriminative choice behavior in both 15 and 23-day-old rat pups, it increased latency to choice in 15-day-old pups and decreased latency to choice in 23-day-olds. This disruption of discriminated choice behavior was not due to differential shock thresholds or differences in locomotor behavior between drug treated and control animals, nor was it specific to a T-maze shock/escape discrimination task. Results suggest that central cholinergic mediation of different behaviors may mature at different rates. 26 references. (Author abstract)

002382 Svenson, Erland; Persson, Lars-Olaf; Sjöberg, Lennart. Institute of Aviation Medicine, National Defense Research Institute, Dept. 5, S-58013 Linköping, Sweden **Mood effects of diazepam and caffeine**. *Psychopharmacology*. 67(1):73-80, 1980.

Changes in mood after administration of diazepam and caffeine to 23 human volunteers were investigated. Six aspects were studied: pleasantness, activation, extraversion, calmness, social orientation, and control. In addition to this check list procedure, mood ratings using magnitude estimation of selected adjectives were obtained. It was found that diazepam decreased feelings of activation and extraversion and increased calmness. Caffeine had no clear effects on the check list, but on the magnitude estimation scale, some effects opposite to those of diazepam were observed. Men reported a higher degree of pleasantness than women after administration of diazepam. No differences in heart rate were found. Few distance scale values were utilized on the magnitude estimation scale and the discriminative power was found to be larger for the check list than for the magnitude estimation scale. 29 references. (Author abstract modified)

002383 van Ree, J. M. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Vondellaan 6, 3521 GD Utrecht, The Netherlands **Reinforcing stimulus properties of drugs**. *Neuropharmacology*. 18(12):963-969, 1979.

The use of self-administration procedures in animals to determine the reinforcing stimulus properties of psychoactive drugs and to predict quantitatively and qualitatively their abuse potential in humans is discussed. External factors such as dose, schedule of drug availability, and stimulus control are critically important in the initiation, maintenance, and cessation of self-administration behavior. Drug-induced changes in the organism,

including tolerance and physical dependence, may contribute to the behavior associated with drug use and consequently alter the pattern of drug intake. Internal factors may also be involved in the control of drug seeking behavior: addictive drugs may mimic the action of endogenous substances involved in the physiological mechanisms underlying reinforcement. Neuropeptides involved in adaptation to the environment may modulate the consequences of drug self-administration by interfering with the interaction of addictive drugs with brain homeostatic mechanisms, and derangements in neuropeptide systems may be critical factors in the development of addictive behavior. 53 references. (Author abstract modified)

002384 Volavka, Jan; Dornbush, Rhea; Mallya, Ashok; Cho, Dong. Missouri Institute of Psychiatry, 5400 Arsenal Street, St. Louis, MO 63139 **Naloxone fails to affect short-term memory in man.** *Psychiatry Research.* 1(1):89-92, 1979.

The effects of naloxone on memory were studied in 26 healthy male volunteers. Either placebo, or 10mg, or 20mg of naloxone was given intravenously on separate occasions. Ten minutes after each injection, the subjects listened to eight lists of words (10 words on each list). Immediate recall, delayed recall, and delayed recognition were not affected by naloxone within 60 minutes of its administration. These results provide no support for the hypothesis that endorphins play a role in the short-term auditory memory in man. 5 references. (Author abstract)

002385 Weingartner, Herbert; Rapoport, Judith L.; Buchsbaum, Monte S.; Bunney, William E., Jr.; Ebert, Michael H.; Mikkelsen, Eward J.; Caine, Eric D. Laboratory of Psychology and Psychopathology, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **Cognitive processes in normal and hyperactive children and their response to amphetamine treatment.** *Journal of Abnormal Psychology.* 89(1):25-37, 1980.

Fourteen normal and 15 hyperactive children were compared on cognitive tasks following placebo or amphetamine administration (.5mg/kg) in a double-blind crossover study. In the undrugged state, normal children remembered more information under free recall retrieval conditions than hyperactive children did, whereas cued recall did not differentiate between these two groups of children. Both normal and hyperactive children demonstrated similar, amphetamine related increases in the recall of semantically and acoustically processed words. This enhancement of cognition occurred along with improvements in attention but was independent of such attentional changes. The pattern of amphetamine-induced changes in cognition is generally similar in normal and hyperactive children. Differences in response to amphetamine that do appear involve components of cognition that distinguish these children in the undrugged state (semantic processing, organization in recall, and free retrieval of information). 38 references. (Author abstract)

002386 Wickstrom, E.; Amrein, R.; Haefelfinger, Pgil.; Hartmann, D. Ullevål Hospital, Avdeling III, Oslo 1, Norway **Pharmacokinetic and clinical observations on prolonged administration of flunitrazepam.** *European Journal of Clinical Pharmacology.* 17(3):189-196, 1980.

Pharmacokinetic and clinical observations on prolonged administration of flunitrazepam and sleep and awakenings were examined in eight patients who were given flunitrazepam (2mg orally) once daily for 28 consecutive days. The time course of the plasma concentration of unchanged flunitrazepam and its principal metabolites were studied in detail after the first and last doses. Additional blood samples were collected immediately before administration of the tablet on days 4, 7, 11, 14, 18, 21, and 25. Clinically, there were no changes during the trial period in the onset of number of spontaneous awakenings, or in the pa-

tients' condition on awakening. The time course of the plasma concentration of flunitrazepam could be described by a three compartment model, assuming that the rate constants remained unchanged during treatment. Maximal plasma concentrations of unchanged flunitrazepam, found 2 hours after intake, reached 10 to 10ng/ml after the first and 15 to 20ng/ml after the last dose. The beta-half-life was found to be between 20 and 36 hours. 13 references. (Author abstract modified)

002387 Wilson, Ian C.; Prange, Arthur J., Jr.; Loosen, Peter T. Prange: Dept. of Psychiatry, Biological Sciences Research Center 220H, University of North Carolina, Chapel Hill, NC 27514 **Psychological and thyroid-stimulating hormone changes after thyrotropin-releasing hormone in normal women: antagonism by pretreatment with thyroid hormones.** *Psychiatry Research.* 2(2):211-222, 1980.

The possible role of thyroid activation in producing the salutary behavioral effects of a single i.v. dose of thyrotropin releasing hormone (TRH) was studied using a double-blind crossover design in which 20 normal women were treated with TRH or saline preceded by 48 hours by a single dose of oral thyroid hormones (TH). TRH caused a shift toward mild euphoria, both on objective and subjective ratings. Although statistically significant, the effect was less than that observed in a previous study of normal women in which TH pretreatment was not used. Thus, TH pretreatment appeared partly to block psychological response to TRH. As expected, TH pretreatment also partly blocked thyroid stimulating hormone (TSH) responses to TRH. Nevertheless, psychological responses were significantly negatively correlated with TSH responses. It is concluded that TH appears to exert two independent negative feedback effects: one on the brain (diminished psychological response) and one on the anterior pituitary (diminished TSH response). 31 references. (Author abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

002388 Alexander, Paul E.; van Kammen, Daniel P.; Bunney, William E., Jr. Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906 **Serum calcium and magnesium levels in schizophrenia: II. Possible relationship to extrapyramidal symptoms.** *Archives of General Psychiatry.* 36(12):1372-1377, 1979.

The relationship between serum calcium and magnesium levels and neuroleptic-induced extrapyramidal symptoms (EPS) was studied in 22 schizophrenic patients. The 16 patients in whom EPS developed had significantly lower mean drug free calcium level than the six patients in whom EPS did not develop. In patients with EPS, drug free serum calcium and magnesium levels together correlated significantly with the neuroleptic dosage at which EPS first developed; lower calcium and magnesium values predicted EPS at lower dosages. In a previous study, it was shown that both serum calcium and magnesium levels were significantly lower during neuroleptic treatment than in the drug free state. In this study, a similar trend was observed, but the calcium value tended to be, and the magnesium value was, significantly lower at the onset of neuroleptic-induced EPS than during the mean of an entire pimozide trial. 54 references. (Author abstract)

002389 Allen, Marcia Divoli; Greenblatt, David J.; Noel, Barbara J. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Self-poisoning with over-the-counter hypnotics.** *Clinical Toxicology.* 15(2):151-158, 1979.

The incidence and consequences of over the counter (OTC) hypnotic overdoses admitted to a large general hospital between 1962 and 1975 were investigated. Drug-induced psychosis is the major consequence of OTC hypnotic poisoning. The psychosis produced by anticholinergic drugs resembles that caused

by sympathomimetic agents or hallucinogens. Different physiological reactions to the toxicity, however, are noted. Physostigmine is the specific antidote for anticholinergic drugs, while phenothiazines are contraindicated. Fatal poisoning due to OTC hypnotics is rare, but acute agitation and delirium are commonly seen in emergency treatment facilities. Intoxication is usually of short duration and responds to conservative management. 9 references. (Author abstract modified)

002390 Ananth, Jambur; Samra, Danny; Kolivakis, Thomas. Allan Memorial Institute, 1025 Pine Ave. West, Montreal, Quebec H3A 1A1, Canada **Amelioration of drug-induced parkinsonism by ECT.** *American Journal of Psychiatry*. 136(8):1094, 1979.

A case study of a 25-year-old man with paranoid schizophrenia who developed severe neuroleptic-induced extrapyramidal symptoms is reported. Eight sessions of bilateral temporo-frontal ECT immediately reduced the extrapyramidal symptoms, thus raising the possibility that ECT may be beneficial in treating such severe symptoms. 4 references.

002391 Antuono, P.; Amaducci, L.; Pazzagli, A.; Pepeu, G. Dept. Neurology, University of Florence, Viale Morgagni, Caruggi, Firenze, Italy **Psychopharmacological perspectives in the treatment of dementia.** *Progress in Neuro-Psychopharmacology*. 3(1-3):75-80, 1979.

Psychopharmacological perspectives in the treatment of dementia are presented, and the relationship between dementias and anticholinergic activity is discussed. It is contended that drugs are among the most frequent causes of dementias, particularly drugs with anticholinergic properties. The similarity between the mental symptoms of anticholinergic poisoning and senile dementia is noted, and the decreased cholinergic activity in postmortem material of Ss with Alzheimer's disease is discussed. The possibility that drugs stimulating brain cholinergic mechanisms might be used in the treatment of dementias is envisaged. 20 references. (Author abstract modified)

002392 Appelbaum, Paul S.; Shader, Richard I.; Funkenstein, H. Harris; Hanson, M. Annette. Shader: Psychopharmacology Research Laboratory, Mass. Mental Health Center, 74 Fenwood Rd., Boston, MA 02115 **Difficulties in the clinical diagnosis of lithium toxicity.** *American Journal of Psychiatry*. 136(9):1212-1213, 1979.

Case reports demonstrating the ease with which lithium toxicity may be confused with other entities are presented. The primary obstacle to early recognition of lithium toxicity in the cases reported was an inappropriately low suspicion of that diagnosis because of lithium levels within the so called therapeutic range. A growing body of literature suggests that elderly patients, schizophrenics, and those with preexisting brain damage may be unusually susceptible to neurotoxicity at therapeutic levels. In the presence of suspicious symptomatology, the serum level alone cannot be used to rule out toxicity. In patients treated with both lithium and a neuroleptic, it is concluded that the heightened side-effects are primarily due to potentiation of lithium neurotoxicity rather than amplification of neuroleptic side-effects by lithium. 10 references.

002393 Asnis, Gregory M.; Asnis, Deborah; Dunner, David L.; Fieve, Ronald R. New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032 **Cogwheel rigidity during chronic lithium therapy.** *American Journal of Psychiatry*. 136(9):1225-1226, 1979.

The presence of extrapyramidal symptoms, especially cogwheel rigidity, was examined in patients receiving lithium alone or in combination with other medications. A neurologic evalua-

tion was given to 97 patients attending a lithium clinic. Cogwheel rigidity and tremor were the main neurologic side-effects noted in this population. The findings suggest that increasing age, lithium level, duration of lithium use, and the presence of tremor predispose patients to or are associated with lithium-induced moderate cogwheeling. The etiology of cogwheel rigidity in lithium treated patients is unclear. It is concluded that this report supports other research in the finding that cogwheel rigidity is occasionally found in manic-depressive patients treated with lithium carbonate. 9 references.

002394 Asnis, Gregory M.; Nathan, R. Swami; Davies, Sharon O.; Halbreich, Uriel. Dept. of Psychiatry, College of Physicians and Surgeons, Columbia University, 722 West 168th Street, New York, NY 10032 **Tardive dyskinesia presenting as a psychosis.** *Journal of Nervous and Mental Disease*. 167(12):762-763, 1979.

A case report of tardive dyskinesia (TD), a movement disorder secondary to neuroleptic medication, presenting as a psychosis, is presented, and the detection of tardive dyskinesia is discussed. It is noted that many patients with TD go undetected because: 1) most patients with TD only have a minimally or mildly severe syndrome, which can be difficult to recognize without a structured movement scale; 2) self-report of TD is often inaccurate; and 3) when dyskinetic movements are grossly apparent, clinicians will occasionally misinterpret them as stereotypes, mannerisms, tics, or habits seen in psychiatric illnesses. 9 references.

002395 Baldessarini, Ross J.; Tarsy, Daniel. Mailmen Laboratories for Psychiatric Research, McLean Division of Massachusetts General Hospital, Belmont, MA 02178 **Dopamine and the pathophysiology of dyskinesias induced by antipsychotic drugs.** *Annual Review of Neuroscience*. 3:23-41, 1980.

The recent clinical and research literature concerning dopamine and the pathophysiology of dyskinesias induced by antipsychotic drugs is reviewed. Topics discussed include: neurologic effects of antipsychotic drugs, acute dystonias, Parkinsonism, akathisia; empirical development of antipsychotic agents; antiparkinsonian actions of antipsychotic agents; clinical features of tardive dyskinesia; presynaptic mechanisms in dopamine overactivity; postsynaptic mechanisms in dopamine overactivity; evaluation of the dopamine supersensitivity hypothesis; and neuropathology in tardive dyskinesia. 97 references.

002396 Ban, T. A. Tennessee Neuropsychiatric Institute, 1501 Murfreesboro Road, Nashville, TN 37217 **Adverse effects in maintenance treatment: practical and theoretical considerations.** *Progress in Neuro-Psychopharmacology*. 3(1-3):231-244, 1979.

Adverse effects of long-term pharmacotherapy with psychotropic drugs are reviewed, and possible negative effects of the increase in fertile marriages among community based patients are discussed. It is noted that in spite of the considerable higher risk for relapse after discontinuation of maintenance therapy, a substantially large percentage of psychiatric outpatients terminate their psychotropic medication. While discontinuation of maintenance therapy may produce relapse in a considerable percentage of patients, continuation of maintenance therapy may lead to drug interaction problems in case of intercurrent illness which requires pharmacological treatment; it may also lead to long-term (chronic) adverse (toxic) effects. Side-effects, teratogenic effects, and cytogenetic effects of neuroleptics and lithium salts are reviewed. 98 references. (Author abstract modified)

002397 Ben-Arie, O.; George, G. C. W. Dept. of Psychiatry, University of Cape Town, Cape Town, Republic of South Africa **A case of tranylcypromine** (*British Journal of Psychiatry*. 135(September):273-274, 1979.

A case of addiction to tranylcypromine is described where tolerance occurred and a severe withdrawal illness followed discontinuation of the drug. The patient was a 47-year-old Caucasian male with a history of emotional deprivation and family instability in childhood. The clinical course described serves as a warning that sedating neuroleptic medication may be insufficient cover for withdrawal of tranylcypromine and that consideration in similar cases should be given to gradual withdrawal of medication. The danger of using amphetamine derivatives in dependence prone personalities is emphasized. Previous reports in the literature of similar cases are reviewed and comparisons made, and the implications for management are discussed. 6 references. (Author abstract modified)

002398 Bender, David A. Courtauld Institute of Biochemistry, Middlesex Hospital Medical School, London, WIP 7PN, England **Inhibition in vitro of the enzymes of the oxidative pathway of tryptophan metabolism and of nicotinamide nucleotide synthesis by benserazide, carbidopa and isoniazid.** *Biochemical Pharmacology*. 29(5):707-712, 1980.

The effects of three hydrazine derivatives on the enzymes of the tryptophan oxidative pathway and of nicotinamide nucleotide synthesis have been studied using preparations from rat liver. The compounds used were benserazide and carbidopa, two inhibitors of aromatic amino acid decarboxylase used together with dopa in the treatment of Parkinson's disease, and the antitubercular agent isoniazid. All three drugs inhibited tryptophan oxygenase and kynureninase, at concentrations that are likely to be encountered in vivo following administration to patients or experimental animals. Isoniazid, but not benserazide or carbidopa, also inhibited 3-hydroxy-anthranilate oxidase and nicotinamide phosphoribosyltransferase. However, these two enzymes were only inhibited significantly at concentrations of the drug far in excess of those likely to be encountered in vivo. On the basis of the in vitro enzyme inhibition studies, it is not possible to explain why patients treated with isoniazid (without supplementary vitamin B6) develop clinical pellagra, while those treated with benserazide or carbidopa do not, despite biochemical evidence of niacin deficiency. It is suggested that this difference may be due either to differences in the intake of dietary niacin in these two groups of patients, or more probably to differences in the metabolism of the drugs and in their interactions with enzymes in vivo that are not apparent in vitro. 18 references. (Author abstract)

002399 Bengtsson, C.; Lennartsson, J.; Lindquist, O.; Noppa, H.; Sigurdsson, J. Dept. of Medicine II, Sahlgrenska Sjukhuset, University of Goteborg, S-431 45 Goteborg, Sweden **Sleep disturbances, nightmares and other possible central nervous disturbances in a population sample of women, with special reference to those on antihypertensive drugs.** *European Journal of Clinical Pharmacology*. 17(3):173-177, 1980.

Sleep disturbances, nightmares, and other possible CNS disturbances in a population sample of women are discussed in relation to the use of antihypertensive drugs. Of 1,302 women aged 44 to 66 years in a population study in Goteborg, Sweden, during 1974 to 1975, 165 were taking antihypertensive drugs, mostly beta-blockers and diuretics. The prevalence of sleep disturbances, nightmares, tiredness and melancholia or depression was compared between women taking antihypertensive medication and those women not taking antihypertensive medication. No difference was found between women taking or not taking various types of single drug therapy or combinations of antihypertensive drugs. In the entire population sample, no significant differences were found among the various age strata, although with increasing age there was a trend towards fewer complaints of nightmares, but a larger number of sleep disturbances as a whole. 12 references. (Author abstract modified)

002400 Bertilsson, Leif; Hojer, Bengt; Tybring, Gunnel; Osterloh, John; Rane, Anders. Dept. of Clinical Pharmacology, Huddinge Hospital, S-141 86 Huddinge, Sweden **Autoinduction of carbamazepine metabolism in children examined by a stable isotope technique.** *Clinical Pharmacology and Therapeutics*. 27(1):83-88, 1980.

Autoinduction of carbamazepine (CBZ) metabolism was investigated in three epileptic children (10 to 13 years of age) using tetradeuterium labeled CBZ (CBZ-D4). Prior to treatment, CBZ and CBZ-D4 given as a mixture had almost identical kinetics in each patient. During maintenance therapy with CBZ, part of the CBZ was exchanged for CBZ-D4 on three occasions. The clearance of CBZ-D4 given on the second day of therapy was 0.036, compared to 0.0281/kg/hour prior to treatment. Clearance doubled after 17 to 32 days of treatment, but no further increase was seen in the next 4 months. 18 references. (Author abstract modified)

002401 Black, James A.; Golden, Gregory T.; Fariello, Ruggero G. Fariello: Clinical Science Center, 600 Highland Ave., H4/621, Madison, WI 53792 **Ketamine activation of experimental corticoreticular epilepsy.** *Neurology*. 39 30(3):315-318, 1980.

Generalized corticoreticular epilepsy was established in adult cats by parenteral penicillin and electroencephalographic monitoring was carried out to study ketamine activation and the concept of dissociative anesthesia. Ketamine CCl was injected intravenously in doses of 2.5 to 20mg/kg. The findings suggest caution in the clinical use of ketamine in patients with such epilepsy. Because analogous effects have been observed with corticoreticular epilepsy upon administration of GABA-mimetic agents, GABA systems may play a role in ketamine anesthesia and corticoreticular epilepsy. Precollateral brain transections did not modify ketamine effects, excluding a possible influence of mesencephalic centers on the observed potentiation. 24 references. (Author abstract modified)

002402 Blum, Alexander. V.A. Medical Center, 3801 Miranda Ave., Palo Alto, CA 94304 **Patients at risk of developing severe side effects from depot fluphenazine treatment.** *American Journal of Psychiatry*. 137(2):254-255, 1980.

The possible range and severity of adverse side-effects from depot fluphenazine treatment of psychoses is illustrated in a case report. Data were obtained from 311 patients receiving such treatment, and results suggest that those with affective disorders may have a propensity to develop severe side-effects, including extrapyramidal symptoms. If schizophrenic patients with these side-effects are reassessed, the findings may reveal an undiagnosed atypical affective disorder which contraindicates depot fluphenazine treatment. 8 references.

002403 Blumenthal, Monica D.; Davie, James W. Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15261 **Dizziness and falling in elderly psychiatric outpatients.** *American Journal of Psychiatry*. 137(2):203-206, 1980.

A group of 100 psychiatric patients who were 60 years old and older were examined for orthostatic hypotension and symptoms of dizziness and falling. Almost 40% of the Ss complained of dizziness and falling, although only 27% had systolic orthostatic hypotension. Drug treatment, particularly the combination of tricyclics with other orthostatic hypotension inducing drugs, was the most important factor accounting for the dizziness and falling. Underlying medical illness, particularly heart disease, also correlated significantly with patients' symptoms. 23 references. (Author abstract modified)

002404 Bone, Stanley; Roose, Steven P.; Dunner, David L.; Fieve, Ronald R. New York State Psychiatric Institute, 722

West 168th Street, New York, NY 10032 **Incidence of side effects in patients on long-term lithium therapy.** *American Journal of Psychiatry.* 137(1):103-104, 1980.

A survey of patients at the New York State Psychiatric Institute Lithium Clinic was conducted in order to evaluate the instance and severity of several lithium side-effects. Analysis of the questionnaires and interviews indicated that while certain side-effects (hand tremor, excessive urination, dry mouth, and thirst) were common, they were seldom perceived as severe by the patient. Patients who were depressed or manic complained more frequently of side-effects than those who were euthymic. Patients receiving psychotropic medications in addition to lithium reported a greater incidence and severity of side-effects than did patients with normal or dysphoric moods on lithium alone. 6 references.

002405 Bourgeois, M.; Bouilh, P.; Tignol, J.; Yesavage, J. Yesavage: Dept. of Psychiatry, Stanford University Medical School, Stanford, CA 94305 **Spontaneous dyskinesias vs. neuroleptic-induced dyskinesias in 270 elderly subjects.** *Journal of Nervous and Mental Disease.* 168(3):177-178, 1980.

Spontaneous dyskinesias and neuroleptic-induced dyskinesias were compared in 270 elderly subjects of a retirement home in France. Females were found to have twice the incidence of dyskinesias than did males. In addition, 18 percent of the patients who had not received neuroleptics had dyskinesias, and 42 percent of those who had received neuroleptics had dyskinesias. This difference is significant at the p equals .0001 level. The results are discussed in terms of the general phenomena of central nervous system degeneration in the elderly. 8 references. (Author abstract modified)

002406 Bremness, Andrew B.; Sverd, Jeffrey. Division of Child Psychiatry, State University of New York, Health Sciences Center, T-10, Stony Brook, NY 11794 **Methylphenidate-induced Tourette syndrome: case report.** *American Journal of Psychiatry.* 136(10):1334-1335, 1979.

A report of a clear case of methylphenidate-induced Tourette syndrome in a child not previously treated with psychoactive medications is presented. The patient, a 9.5-year-old boy who was referred for behavioral problems that included aggressiveness, was diagnosed as having a hyperactive/aggressive behavioral disorder. Treatment was started with a combination of behavioral therapy and methylphenidate. After about 10 weeks on the maximum dose of 60mg/day, the child developed multiple tics and vocal productions that progressed to a fully developed Tourette syndrome. When the Tourette symptoms appeared the medication was stopped. A 90% symptom resolution was reported in the first days after cessation but reappeared 5 weeks after discontinuation of methylphenidate. It is concluded that the case verifies a serious side-effect of methylphenidate treatment. 8 references.

002407 Brown, Walter A.; Laughren, Thomas P. Dept. of Psychiatry, Brown University, Providence, RI 02912 **Growth-hormone release and the tardive dyskinesia of neuroleptic withdrawal.** *Lancet.* No.8162:259, 1980.

The effects of withdrawal from neuroleptic drugs were studied in 21 men with chronic schizophrenia and in four who had other psychiatric syndromes, dominated by anxiety. After withdrawal, patients were evaluated weekly with blood samples, psychological evaluation, and completion of an abnormal involuntary movement scale. Serum was assayed for growth hormone (GH), cortisol, and prolactin by radioimmunoassay. Patients with tardive dyskinesia on neuroleptic medication showed sustained GH increases, while those with chronic tardive dyskinesia and those without dyskinesia maintained normal GH

levels during drug withdrawal. It is concluded that the withdrawal of neuroleptic medication is associated in some patients with endocrine ramifications which, though apparently transient, may have clinical implications in patients with underlying endocrine and metabolic disorders. 1 reference.

002408 Burnett, Gordon B.; Prange, Arthur J., Jr.; Wilson, Ian C.; Jolliff, Lula A.; Creese, Ian C.; Snyder, Solomon H. Dept. of Psychiatry, Division of Health Affairs, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Adverse effects of anticholinergic antiparkinsonian drugs in tardive dyskinesia: An investigation of mechanism.** *Neuropsychobiology.* 6(2):109-120, 1980.

A total of 10 long-term schizophrenic patients with tardive dyskinesia were studied over 14 weeks and maintained on their usual neuroleptic medications while anticholinergic antiparkinsonian drugs were employed and then discontinued. Discontinuation of anticholinergic medications resulted in improvement in dyskinetic movements. Estimation of haloperidol equivalents in serum at four times suggested that changes in severity of tardive dyskinesia were not caused by changes in blood levels of neuroleptics. Levels of pituitary hormones were also estimated at four times. Prolactin levels tended to diminish in men over the course of the experiment. Growth hormone and thyrotropin values were mainly stable. However, the growth hormone levels peaked during the final off anticholinergic condition and thyrotropin levels were consistently elevated. The main finding of the study, that standard anticholinergic antiparkinsonian medication aggravates tardive dyskinesia, is confirmed by previous research. 52 references. (Author abstract modified)

002409 Caine, Eric D.; Polinsky, Ronald J. Dept. of Psychiatry, University of Rochester Medical Center, 300 Crittenden Blvd., Rochester, NY 14642 **Haloperidol-induced dysphoria in patients with Tourette syndrome.** *American Journal of Psychiatry.* 136(9):1216-1217, 1979.

Haloperidol-induced dysphoria in patients with Tourette syndrome is discussed and some case histories presented. In a population of 72 patients, six were found to suffer this response to haloperidol. The phenomenon was not related to drowsiness and cognitive impairment. The absence of akinesia tends to exclude the depression associated with this side-effect. The effective suppression of involuntary motor and vocal tics may have resulted from dopamine receptor blockade in the basal ganglia. It is suggested that the changes in mood state were the result of the altered dopamine mediated neurotransmission in the mesolimbic dopaminergic pathway. 3 references.

002410 Cameron, Oliver G.; Wimer, Linda. Dept. of Psychiatry, University of Michigan, 1405 E. Ann Street, Ann Arbor, MI 48109 **An anticholinergic toxicity reaction to chlorpromazine activated by psychological stress.** *Journal of Nervous and Mental Disease.* 167(8):508-510, 1979.

A case in which a change in environmental status apparently increased stress on a patient and, when coupled with a dosage of chlorpromazine which had been well tolerated previously, resulted in a toxic confusional reaction is reported. A 42-year-old woman with a long standing diagnosis of schizophrenia experienced two toxic reactions to 1200mg of chlorpromazine while awaiting surgery for a locally metastatic carcinoma of the cervix. These reactions, which involved fever, increased pulse and respirations, and acute onset of obtundation, and which cleared after several hours, were produced by a medication and dose which had been well tolerated prior to the preoperative period. These reactions, typical of an acute anticholinergic syndrome, were precipitated by an interaction of the drug and a stress-induced change in her psychological state, due to anxiety

about her cancer and impending surgery. 13 references. (Author abstract modified)

002411 Camfield, Peter R.; Bagnell, Philip; Camfield, Carol S.; Tibbles, J. A. R. Izaak Walton Killam Hospital for Children, Halifax, Nova Scotia, Canada B3J 3G9 **Pancreatitis due to valproic acid.** *Lancet*. No. 8127:1198-1199, 1979.

Two cases of children with attacks of pancreatitis following exposure to valproic acid are discussed. Recovery followed shortly after termination of the administration of valproic acid. Serum amylase was measured in 10 other symptom free children who had been taking valproic acid for from 2 to 14 months. These determinations were normal. Pancreatic dysfunction may play a role in the abdominal discomfort and vomiting seen in about a fifth of patients taking valproic acid. It is suggested that valproic acid be discontinued in any child with clinical or laboratory evidence of pancreatic disease. Routine serum amylase determinations are recommended for patients with abdominal symptoms who are using this drug.

002412 Caroff, Stanley N. V.A. Hospital, 151-E, University and Woodland Avenues, Philadelphia, PA 19104 **The neuroleptic malignant syndrome.** *Journal of Clinical Psychiatry*. 41(3):79-83, 1980.

The clinical characteristics and differential diagnoses of the neuroleptic malignant syndrome (NMS), an underdiagnosed but potentially lethal consequence of treatment with powerful neuroleptics, are described. A review of the literature is included, and the need for further studies of the incidence, etiology, and pathogenesis of the NMS is emphasized. Such studies are necessary to enhance knowledge of neuroleptic pharmacology and produce more effective means of prevention and treatment. 31 references. (Author abstract modified)

002413 Chadwick, D. W.; Cumming, W. J. K.; Livingstone, I.; Cartledge, N. E. F. Dept. of Neurology, Royal Victoria Infirmary, Newcastle upon Tyne NE4 1LP, England **Acute intoxication with sodium valproate.** *Annals of Neurology*. 6(6):552-553, 1979.

The cases of two epileptic patients who developed an acute toxic encephalopathy consisting of altered behavior, deteriorating seizure control, and confusion while taking valproate alone are reported. Serum valproate levels were greater than 100mcg/ml in both. It is reported that toxic symptoms resolved when the dose of valproate was reduced, with a consequent fall in serum concentration of the drug. 6 references. (Author abstract modified)

002414 Charney, Dennis S.; Kales, Anthony; Soldatos, Constantine R.; Nelson, J. Craig. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Somnambulistic-like episodes secondary to combined lithium-neuroleptic treatment.** *British Journal of Psychiatry*. 135(November):418-424, 1979.

Ten of 114 psychiatric patients undergoing combined lithium/neuroleptic treatment who exhibited somnambulistic-like episodes are reported on. These episodes are differentiated from nocturnal wanderings and epileptic attacks during sleep; they occurred within 2 to 3 hours after sleep onset and were characterized by the patients appearing confused and walking about in a quiet, detached, and clumsy manner. Generally, there was amnesia for the event. Since sleepwalking occurs out of slow wave sleep, the increase in slow wave sleep induced by lithium and certain neuroleptics may represent a neurophysiological mechanism responsible for these patients' somnambulistic behavior. The occurrence of grand mal seizures in two patients was probably unrelated to the somnambulistic-like episodes. However,

persistence of the latter appears to be associated with drug-induced EEG irregularity. 34 references. (Author abstract)

002415 Chouinard, Guy; Jones, Barry D. Research Dept., Hospital Louis-H. Lafontaine, 7401 rue Hochelaga, Montreal, Quebec, Canada H1N 3M5 **Early onset of tardive dyskinesia: case report.** *American Journal of Psychiatry*. 136(10):1323-1324, 1979.

A case report of a patient who developed tardive dyskinesia one month after his first exposure to neuroleptic drug treatment is reported. The patient was a 23-year-old male who first received psychiatric treatment for complaints of depression. Originally he was treated in an outpatient psychotherapy setting without medication. When this treatment was unsuccessful he received trifluoperazine and chlorpromazine. After only 1 month of medication he developed tardive dyskinesia. The early onset of the disorder was detected because there was a relative absence of hypokinetic parkinsonian symptoms thus facilitating early detection. The antiparkinsonian drug the patient received could also have contributed to the early emergence of dyskinetic movements. The possibility of tardive dyskinesia developing in patients who have been taking neuroleptic drugs for a relatively short time contraindicates neuroleptic use in the treatment of nonpsychotic patients. 9 references.

002416 Chouinard, Guy; Jones, Barry D. Research Department, Hospital Louis-H. Lafontaine, 7401 rue Hochelaga, Montreal, Quebec, Canada H1N 3M5 **Neuroleptic-induced supersensitivity psychosis: clinical and pharmacologic characteristics.** *American Journal of Psychiatry*. 137(1):16-21, 1980.

Ten cases of neuroleptic-induced supersensitivity disorder are described which illustrate the pharmacologic and clinical characteristics of the syndrome which is a supersensitivity syndrome induced by long-term use of neuroleptic drugs. Seven characteristics of the syndrome are described. It is concluded that an implication of neuroleptic-induced mesolimbic supersensitivity is that the tendency toward psychotic relapse in such patients is determined by more than just the normal course of the illness. 15 references. (Author abstract modified)

002417 Cloyd, James C.; Gumint, Robert J.; Lesar, Timothy S. Dept. of Pharmaceutical Services, St. Paul-Ramsey Medical Center, 640 Jackson Street, St. Paul, MN 55101 **Reduced seizure control due to spoiled phenytoin capsules.** *Annals of Neurology*. 7(2):191-193, 1980.

Subtherapeutic phenytoin serum levels and loss of seizure control occurred in a 31-year-old man due to decreased bioavailability of oral drug caused by spoilage of phenytoin capsules. During storage at extreme temperatures, physical changes of the phenytoin capsule resulted in altered dissolution characteristics so that only 50% dissolution occurred at 180 minutes compared with 95% in 120 minutes for control capsules. Similar changes were produced in fresh capsules within 7 days at high temperature and humidity. The affected patient has metabolic responses to phenytoin that produced marked fluctuations in serum levels with changes in dose. Altered phenytoin serum concentrations may occur with minor dose changes in such patients despite good compliance. 10 references. (Author abstract modified)

002418 Cohen, Robert M.; Pickar, David; Murphy, Dennis L. NIH Clinical Center, Bldg. 10, Rm. 3D48, Bethesda, MD 20205 **Myoclonus-associated hypomania during MAO-inhibitor treatment.** *American Journal of Psychiatry*. 137(1):105-106, 1980.

A case study of a man who developed myoclonus associated with hypomania while receiving monoamine oxidase inhibitors for the treatment of depression is reported. The simultaneous occurrence of hypomania with myoclonus suggests that some of

the pathways involved in these phenomena may be shared. The patient's reactions indicate that an epileptic-like foci is involved in the activation of behavior. It is concluded that neurobiologic dysregulation is an important central concept in the understanding of the activity of antidepressant drugs. 10 references.

002419 Coppen, A.; Ghose, K.; Jorgensen, A. Medical Research Council Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey KT19 8PB, England **Pharmacokinetics and pharmacodynamics of amitriptyline in depression.** *Progress in Neuro-Psychopharmacology*. 3(1-3):191-199, 1979.

The therapeutic effect and pharmacokinetics of amitriptyline were assessed in thirty-five patients suffering from primary depressive illness during inpatient treatment. Contrary to results of previous studies, no significant correlation was obtained between the plasma concentrations of amitriptyline, nortriptyline, or total tricyclics with Hamilton rating scores at 6 weeks or percentage improvement after 6 weeks treatment. No relationship between plasma concentration of tricyclics and side-effects was found, but a linear correlation was observed between the plasma concentration of nortriptyline and decreased tyramine sensitivity, and index of noradrenaline reuptake blocking effect. Patients who complained of more side-effects had less clinical benefit during amitriptyline therapy. 16 references. (Author abstract modified)

002420 Coryell, William; Sherman, Arnold. Dept. of Psychiatry, University of Iowa College of Medicine, 500 Newton Rd., Iowa City, IA 52242 **Slow tricyclic antidepressant metabolism, polypharmacy, and cardiac arrest.** *American Journal of Psychiatry*. 137(1):108-109, 1980.

A case history of a woman whose cardiac arrest and high plasma tricyclic level led to the initial assumption of an intentional overdose is reported. Further examination and study indicated that her cardiac arrest resulted from her slow tricyclic antidepressant metabolism and adverse drug interactions. She was advised to avoid future tricyclic antidepressant medications. 9 references.

002421 Coulter, David L.; Allen, Richard J. Section of Pediatric Neurology, Dept. of Pediatrics and Communicable Diseases, University of Michigan Medical Center, Ann Arbor, MI 48109 **Pancreatitis associated with valproic acid therapy for epilepsy.** *Annals of Neurology*. 7(1):92, 1980.

Cases of pancreatitis associated with valproic acid therapy for epilepsy in children are reported. One patient recovered from the first episode of pancreatitis while taking phenytoin alone, suggesting that this drug was not the cause of his illness. Three months later, reinitiation of valproic acid was associated with a recurrence of pancreatitis. Four other patients have recently been reported who developed pancreatitis from valproic acid. It is concluded that the present evidence suggests that pancreatitis is associated with the use of valproic acid for seizures. 5 references.

002422 Crome, Peter; Newman, Belinda. Poisons Unit, Guy's Hospital, London SE1 9RT, England **Fatal tricyclic antidepressant poisoning.** *Journal of the Royal Society of Medicine*. 72(9):649-653, 1979.

A survey of all deaths due to tricyclic antidepressant poisoning in the United Kingdom was conducted in a single year to ascertain the epidemiological and clinical features. In 1976, 345 deaths were reported due to tricyclic antidepressants; 42.6% of the patients were aged between 40 and 59 and women outnumbered the men in the ratio 1.6:1. Amitriptyline accounted for over half the deaths. Of the 135 patients dying in hospital, coma, hypotension, and sinus tachycardia were the commonest

presenting symptoms. It is indicated by the survey that the importance of cardiac arrhythmias has been overestimated and the importance of respiratory depression underestimated in the management of severe tricyclic poisoning. It is suggested that, although most deaths occur outside the hospital, better application of the principles of intensive supportive care could reduce the hospital mortality. 14 references.

002423 Davies, B.; Kincaid-Smith, Priscilla. Dept. of Psychiatry, University of Melbourne, Royal Melbourne Hospital, Victoria 3050, Australia **Renal biopsy studies of lithium and prelithium patients and comparison with cadaver transplant kidneys.** *Neuropharmacology*. 18(12):1001-1002, 1979.

Renal biopsies were performed on 16 patients who had been taking lithium regularly for a mean of 5.5 years, 9 patients about to begin lithium prophylaxis, and an age matched sample of cadaver donor kidneys. Specific tubular lesions were found only in the patients receiving lithium. These lesions developed within a few days of starting lithium and appeared to be reversible. Since the lesions were located in a region believed to be rich in vasopressin receptors, they may be the pathological basis of the vasopressin resistant diabetes insipidus syndrome seen in patients on lithium. Nonspecific changes were found in biopsy material from all three groups. The only normal prelithium biopsy was obtained from the sole prelithium patient who had never received major tranquilizers or antidepressants, which suggests that these drugs may also have nephrotoxic effects. 3 references.

002424 Dodson, W. Edwin. St. Louis Children's Hospital, 500 South Kingshighway, P.O. Box 14871, St. Louis, MO 63178 **Phenytoin elimination in childhood: effect of concentration-dependent kinetics.** *Neurology*. 30(2):196-199, 1980.

The effect of phenytoin (PHT) concentration on the elimination rate of PHT and effective half-life was evaluated in epileptic children and young adults and children accidentally poisoned with PHT (age range from 1 day to 22 years). As PHT concentration increased, the effective half-life increased. In eight children, aged 7 months to 4.83 years with initial concentrations between 10 to 20mg/liter, the average half-life (18.6 hours) was approximately 58% as long as the average in adults with comparable concentrations. Whereas the half-life correlated with the initial PHT concentrations, there was no correlation overall between half-life and age, size, or number of other antiepileptic medications taken. The concentration dependence of the half-life provided the basis for less frequent dosing than one would expect from previous studies of PHT half-life in children with low concentrations. 18 references. (Author abstract modified)

002425 Doss, Faye W. Suite 512, 801 Princeton Avenue, P.O. Box 3627, Birmingham, AL 35211 **The effect of antipsychotic drugs on body weight: a retrospective review.** *Journal of Clinical Psychiatry*. 40(12):528-530, 1979.

The effect of antipsychotic drugs on bodyweight was examined in a retrospective review of 78 schizophrenic patients. Results revealed that thiothixene, fluphenazine, haloperidol, and thioridazine produced a mean weight gain and loxapine a mean weight loss after 12 and 36 weeks of treatment. The ability of an effective antipsychotic drug, such as loxapine, to prevent weight gain or to produce weight loss offers a clinical advantage in the treatment of those schizophrenic patients in whom weight gain would be a problem. 32 references. (Author abstract modified)

002426 Downing, R. W.; Rickels, K.; Rickels, L. A.; Downing, D. 203 Piersol Building, Hospital of the University of Pennsylvania/G1, 3400 Spruce St., Philadelphia, PA 19104 **Nonspecific factors and side effect complaints: factors affecting the incidence of drowsiness in drug and placebo treated anxious and depressed outpatients.** *Acta Psychiatrica Scandinavica*. 60(5):438-448, 1979.

Discriminant function analyses were applied to data obtained from anxious psychiatric outpatients treated with either chlor-diazepoxide or placebo and depressed outpatients treated with either amitriptyline or placebo. The 1,250 subjects had participated in 4-week long controlled drug trials in an attempt to identify factors associated with complaints of drowsiness. Although the magnitude of the relationships between individual predictors and drowsiness was small, several factors emerged which had consistent impact across treatment groups. Predictors of complaints of drowsiness attributed to active drugs arose primarily from demographic attributes probably reflective of life style, and from illness and treatment history. In contrast, predictors of drowsiness attributed to placebo were almost exclusively confined to indices of the severity of several aspects of presenting symptomatology. In particular, more frequent complaints of drug-induced drowsiness were found among better educated individuals with an illness of long duration. 18 references. (Author abstract modified)

002427 Edwards, J. Guy. Royal South Hants Hospital, Southampton, SO9 4PE, England **Antidepressants and convulsions**. *Lancet*. No. 8156/7:1368-1369, 1979.

The incidence of seizures and related problems in patients taking antidepressants was studied. Background data on patients whose seizures have allegedly been caused by mianserin were collected. mentally subnormal patient who was reported as having had grand-mal attacks while taking mianserin had malignant hypertension and hypertensive retinopathy. In another case the patient was suspected of having an organic brain disease which itself could have caused the attack. A third patient, an alcoholic, was withdrawing from large dosages of diazepam when the seizure happened. In other instances patients were concurrently receiving other potentially epileptogenic drugs or were being withdrawn from benzodiazepines. It is suggested that the accuracy and usefulness of reports can be increased if those reporting data on seizures provide more detail, including information on preexisting disorders predisposing to epilepsy, the concomitant use of other potentially epileptogenic drugs, and withdrawal from drugs and/or alcohol. 5 references.

002428 Einarson, Thomas R.; Tyrer, P. Dept. of Pharmacy, General and Marine Hospital, Owen Sound, Ontario, Canada N4K 5H3 **Lorazepam withdrawal seizures**. *Lancet*. No. 8160:151, 1980.

In two letters to the editor, the effects of taking mianserin and of withdrawal from lorazepam on grand mal seizures are discussed. Several case histories are mentioned to support arguments that one but not both drugs are responsible for the seizures. It is argued that outpatients, some with abnormal personalities, do not have an accurate history of drug ingestion or abuse. The combination of mianserin treatment and lorazepam withdrawal probably was responsible for at least one grand mal seizure. It is concluded that mianserin is possibly epileptogenic. 14 references.

002429 Evans, Dwight L.; Martin, Willis. Dept. of Psychiatry, University of North Carolina, North Carolina Memorial Hospital, Chapel Hill, NC 27514 **Lithium carbonate and psoriasis**. *American Journal of Psychiatry*. 136(10):1326-1327, 1979.

A case history of a 27-year-old male who developed psoriasis during treatment with lithium carbonate is reported. A relationship between lithium carbonate and psoriasis has been noted by several authors. The patient in the case history was treated with lithium carbonate when he developed hypomanic behavior. About 3 months after initiation of lithium carbonate therapy he developed psoriasis. As in other cases where such data has been reported, skin exacerbation occurred soon after initiation of lithium

therapy. Serum lithium levels were in the therapeutic range. The psoriasis proved refractory to traditional topical antipsoriatic therapy. Other dermatologic conditions have been observed in patients treated with lithium. Whether there is a causal link between lithium therapy and the onset and/or exacerbation of psoriasis is yet to be determined. 10 references.

002430 Extein, Irl; Potter, William Z.; Wehr, Thomas A.; Goodwin, Frederick K. Neuropsychiatric Evaluation Unit, Fair Oaks Hospital, 19 Prospect St., Summit, NJ 07901 **Rapid mood cycles after a noradrenergic but not a serotonergic antidepressant**. *American Journal of Psychiatry*. 136(12):1602-1603, 1979.

A case of rapid mood cycles developing in a depressed patient in response to treatment with desipramine but not in response to zimelidine is reported. A significant percentage of depressed patients with bipolar illness have been known to switch into mania after treatment with antidepressants and to experience rapid mood cycles if the medication is maintained. The findings in the case of a 57-year-old woman are discussed in terms of theories about the selective involvement of norepinephrine and 5-hydroxytryptamine in mood disorders. 10 references.

002431 Gelenberg, Alan J. Dept. of Psychiatry, Massachusetts General Hospital, Boston, MA 02114 **Amoxapine, a new antidepressant, appears in human milk**. *Journal of Nervous and Mental Disease*. 167(10):635-636, 1979.

A young woman developed galactorrhea during treatment with a new dibenzoxazepine antidepressant, amoxapine. Both amoxapine and its active and major metabolite, 8-OH-amoxapine, appeared in her milk. More recent literature suggests that probably all antidepressants can appear in human milk. The first sample of milk was collected after 10 months of drug therapy (45 min following her last dose of drug), the other sample was collected after 11 months of drug therapy (11.5 hours after her last dose of drug). 14 references. (Author abstract modified)

002432 Gershon, Samuel; Newton, Roger. Dept. of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016 **Lack of anticholinergic side effects with a new antidepressant -- trazodone**. *Journal of Clinical Psychiatry*. 41(3):100-104, 1980.

The occurrence of anticholinergic side-effects in 15 multicenter studies of 379 patients with endogenous depression who received either trazodone, imipramine, or placebo was investigated. The incidence of four specific anticholinergic side-effects was focused upon. When the number of Ss having each symptom was compared, there were no significant differences in the incidence of side-effects between the trazodone and placebo groups. Comparisons between trazodone and imipramine, however, indicated that the incidence of the side-effects was significantly lower in the trazodone group. 13 references. (Author abstract modified)

002433 Grasso, A.; Alema, S.; Rufini, S.; Senni, M. I. Laboratory of Cell Biology, CNR, Via Romagna 18/A, I-00196 Rome, Italy **Black widow spider toxin-induced calcium fluxes and transmitter release in a neurosecretory cell line**. *Nature*. 283(5749):774-776, 1980.

PC12 cells, derived from rat pheochromocytoma, loaded with labeled DA in a CA2 containing medium containing 1 mM EGTA were exposed to black widow spider toxin (BWSTx). Results indicated that BWSTx produced a rapid and massive influx of CA2 ions in these toxin responsive neurosecretory cells. The main consequence of CA2 influx was the release of neurotransmitters, presumably through a typical exocytic process. Neither NA nor Mg2 alone appeared to effectively substitute for CA2 in inducing transmitter release. Results also con-

firmed and extended previous observations on the antagonistic effect of concavalin A by showing that lectin inhibits BWSTx-induced CA2 uptake. Possible mechanisms enabling the observed CA2 influx are discussed. 22 references.

002434 Harris, Brian; Harper, Max. Dept. of Psychological Medicine, Welsh National School of Medicine, Cardiff CF4 4XN, Wales **Psychosis after dextropropoxyphene**. *Lancet*. No. 8145:743, 1979.

In a letter to the editor, a case of florid psychosis in a 38-year-old woman, admitted after an overdose of tablets (dextropropoxyphene and paracetamol) is reported. It concerned three factors: chronic dependence on Distalgic; sudden increase in intake (overdose); and withdrawal. The patient ingested about 20 tablets. She was found semicomatose and had left a suicide note. Although recovery after stomach washout seemed uneventful, the patient was still very distressed and on the third day psychiatric opinion was sought. She gave a history of increasing depression associated with severe back pain over a 2 year period. On day 4 mianserin was prescribed, 10mg, three times daily. On day 8 an acute psychotic state intervened. On day 9 the psychosis had clear organic features which progressed into a semicomatose condition. By day 10, patient's level of consciousness improved, but severe depression persisted. After the psychotic episode had cleared, the patient was maintained on mianserin for depression. 14 references.

002435 Hartse, Kristyna M.; Roth, Thomas; Piccione, Paul M.; Zorick, Frank J. Sleep Disorders and Research Center, Henry Ford Hospital, Detroit, MI 48202 **Rebound insomnia**. *Science*. 208(4442):423-424, 1980.

Research concerning the phenomenon of rebound insomnia, a worsening of sleep occurring subsequent to the withdrawal of three benzodiazepine hypnotics - flunitrazepam, nitrazepam, and triazolam, is reviewed. Sleep laboratory studies of the rebound insomnia phenomenon in both normal and insomniac populations are reviewed and judged to yield equivocal results. It is contended that more complete data are needed before either the generalizability or specificity of rebound insomnia can be determined. Issues that must be considered include the type of insomniacs who exhibit rebound insomnia, the severity of the insomnia before the drug was prescribed, the specificity of drug withdrawal insomnia to different drug classes, the relationship between rebound insomnia and drug half-lives, and the critical duration of drug administration necessary to produce rebound insomnia upon withdrawal. 11 references.

002436 Hausner, Robert S. Mount Zion-Westside Crisis Center, 1600 Divisadero Street, San Francisco, CA 94115 **Amantadine-associated recurrence of psychosis**. *American Journal of Psychiatry*. 137(2):240-242, 1980.

The recurrence of acute psychosis associated with initiation of amantadine therapy in a patient whose psychotic state had previously been in remission is reported. The patient was being treated for Parkinson's disease, and the hallucinations and psychotic behavior with schizophrenic characteristics were insidious and difficult to recognize, as compared with the side-effects of other major antiparkinsonian drugs. 10 references.

002437 Hes, J. Ph.; Cohn, D. F.; Streifler, M. Dept. of Psychiatry, Sackler School of Medicine, University of Tel Aviv, Tel Aviv, Israel **Ethyl chloride sniffing and cerebellar dysfunction (Case report)**. *Israel Annals of Psychiatry and Related Disciplines*. 17(2):122-125, 1979.

A case of cerebellar disorder is reported in a 28-year-old female with a 4 month history of ethyl chloride (200 to 300 ml/day) inhalation. Presenting symptoms include lassitude, nausea,

abdominal discomfort, dizziness, ataxia, tremor, and dysarthria. The patient had a previous history of addiction, but had been drug free for 2 years before sniffing ethyl chloride. The patient reported both pleasant and unpleasant hallucinations associated with ethyl chloride use. Symptoms fully remitted after 1 month hospitalization. Investigation revealed seven females and one male in the patient's neighborhood who were also using ethyl chloride. Reported toxic effects included disorientation, paranoia, and hallucinations, but cerebellar symptoms were not noted. 8 references. (Author abstract modified)

002438 Heston, Leonard L.; Hastings, Donald. Box 392 Mayo, University of Minnesota Medical School, Minneapolis, MN 55455 **Psychosis with withdrawal from ethchlorvynol**. *American Journal of Psychiatry*. 137(2):249-250, 1980.

Unusual features of the abuse of ethchlorvynol, a widely prescribed sedative hypnotic drug, are described as observed in one patient who was hospitalized for hallucinations following withdrawal from daily doses. These features include the length and severity of the withdrawal syndrome, a period of schizophreniform illness during withdrawal, and an intimate, but complex association between ethchlorvynol and alcohol. 3 references.

002439 Hollender, Marc H.; Ban, Thomas A. Department of Psychiatry, Vanderbilt University Medical School, Nashville, TN 37232 **Ejaculatio retardata due to phenelzine**. *Psychiatric Journal of the University of Ottawa*. 4(3):233-234, 1979.

A case of ejaculatio retardata occurring during the course of the successful treatment of a phobic anxiety depersonalization state with phenelzine, a hydrazine type of MAO inhibitor (60mg daily), is reported. The adverse effect which was probably triggered by an exacerbation of chronic prostatitis, persisted after the infection had cleared. It subsided, however, 3 weeks after the dosage of phenelzine had been reduced to 45mg daily, and it did not recur when the dosage was returned to its former level. It appears that the ejaculatory disorder was due to the interaction of an inflammation induced mechanical obstruction and the MAO inhibitor induced interference with emission mediated by the sympathetic nervous system. 8 references. (Author abstract)

002440 Howell, Edward J. Tulane University School of Medicine, New Orleans, LA 70112 **Sedative and hypnotic overdose**. *Urban Health*. 8(6):11-13, 44-45, 1979.

An overview of sedative and hypnotic overdose factors and management is presented. Guidelines for determining suicidal intent are outlined, and examination and evaluation of the overdose patient are discussed. Incidence, diagnosis, effects, and treatment are considered in overdose cases involving opiates, long-acting and intermediate barbiturates, chloralhydrate, benzodiazepams, meprobromate, phenothiazines, methaqualone, ethchlorvynol, and glutethimide. 21 references.

002441 Husain, Arshad; Chapel, James; Malek-Ahmadi, Parviz. 807 Stadium Road, University of Missouri Medical Center, Columbia, MO 65212 **Methylphenidate, neuroleptics and dyskinesia-dystonia**. *Canadian Journal of Psychiatry*. 25(3):254-258, 1980.

A case history is presented in which the simultaneous use of methylphenidate and a phenothiazine to treat a hyperkinetic patient resulted in serious side-effects following withdrawal of the phenothiazine. It is postulated that phenothiazine treatment caused a postsynaptic supersensitivity which precipitated dystonia and dyskinesia when phenothiazine was withdrawn and methylphenidate was reinstituted. It is concluded that the phenothiazine dopamine blocking action may necessitate use of larger quantities of stimulant to produce the desired treatment effect. 10 references. (Author abstract modified)

002442 Hwang, Sutaeg; Tuason, V. B. Tuason: St. Paul-Ramsey Medical Center, 640 Jackson St., St. Paul, MN 55101 **Long-term maintenance lithium therapy and possible irreversible renal damage.** *Journal of Clinical Psychiatry.* 41(1):11-19, 1980.

The literature regarding structural damage and functional disturbances of the kidneys due to long-term maintenance lithium therapy is reviewed. The correlation between structural changes and functional disturbances of the kidneys is examined. The prognostic implications of lithium-induced nephropathy are discussed, especially in regard to the possible development of chronic renal failure. Recommendations are made to provide maximum benefits of lithium therapy and to minimize accompanying risks of renal side-effects. 84 references. (Author abstract)

002443 Jeste, Dilip V.; Wagner, Richard L.; Weinberger, Daniel R.; Rieth, Kenneth G.; Wyatt, Richard Jed. Intramural Research Program, William A. White Bldg., Room 536, St. Elizabeths Hospital, Washington, DC 20032 **Evaluation of CT scans in tardive dyskinesia.** *American Journal of Psychiatry.* 137(2):247-248, 1980.

Computed tomographic (CT) scans were performed on patients with severe, long lasting dyskinesia and of a matched control group to evaluate conflicting reports of the neuropathology of the disorder. Ss were elderly inpatients and, unexpectedly, there were no significant differences between the two groups. Further studies are needed to determine if chronic neuroleptic treatment itself produces CT scan abnormalities in psychiatric patients. It is tentatively concluded that routine use of CT scans as a diagnostic procedure for tardive dyskinesia for clinical or medicolegal purposes may not be warranted. 10 references.

002444 Jeste, Dilip V.; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, Division of Special Mental Health Research, NIMH, Washington, DC **Tardive dyskinesia: the syndrome.** *Psychiatric Annals.* 10(1):16-19, 22-25, 1980.

An overview of tardive dyskinesia, a syndrome consisting of abnormal stereotyped movements of the mouth, face, tongue, and limbs and occurring rather late in drug treatment, is presented. The nature of tardive dyskinesia and its late and early manifestations are discussed. Diagnostic criteria and differential diagnosis are reviewed; and treatment and patient related factors increasing the risk of tardive dyskinesia are noted. Differentiation of reversible versus persistent tardive dyskinesia and pathophysiology are examined. Prevention and issues of informed consent in neuroleptic treatment are explored. 25 references.

002445 Jones, David R.; Maloney, Thomas R. USAFSAM/NGN, Brooks AFB, TX 78235 **Massive eosinophilic reaction to desipramine.** *American Journal of Psychiatry.* 137(1):115-116, 1980.

A case study of a 52-year-old man who developed a massive eosinophilic reaction to desipramine is reported. The patient developed a clinically significant neutropenia when his eosinophilia reached 81% of a total leucocyte count of 19,000/mm³. All values returned to normal when his medication was changed to nortriptyline. 8 references.

002446 Kales, Anthony; Scharf, Martin B.; Kales, Joyce D.; Soldatos, Constantin R. Sleep Research and Treatment Center, Pennsylvania State University, College of Medicine, Hershey, PA 17033 **Rebound insomnia: a reply to Hartse et al./ Rebound insomnia.** *Science.* 208(4442):424, 1980.

In reply to a review by Hartse et al., Kales et al. reassert that rebound insomnia (a worsening of sleep occurring subsequent to the withdrawal of three benzodiazepine hypnotics -- flunitrazepam, nitrazepam, and triazolam) occurs consistently following the withdrawal of specific benzodiazepine drugs. The criticism

by Hartse et al. that several studies which did not demonstrate rebound insomnia were omitted by Kales et al. from their review is answered. Kales et al. maintain that when one considers the intersubject variability in factors such as drug metabolism and the night to night sleep of insomniacs, as well as the small number of Ss studied in the sleep laboratory, the consistency of rebound insomnia following the withdrawal of certain benzodiazepine drugs is striking. 17 references.

002447 Kim C. S.; O'Tuama, L. A.; Cookson, S. L.; Mann, J. D. Dept. of Neurology, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **The effects of lead poisoning on calcium transport by brain in 30-day-old albino rabbits.** *Toxicology and Applied Pharmacology.* 52(3):491-496, 1980.

The effects of lead poisoning on calcium transport by brain in 30-day-old albino rabbits were investigated. The uptake of ⁴⁵Ca was studied in brain slices that were preincubated for 30 minutes in artificial cerebrospinal fluid (CSF) and then transferred to experimental media. A concentrative uptake of ⁴⁵Ca was not noted: after up to 30 minutes of incubation, T/M ratios were less than 1. Addition of ouabain to the incubation medium in vitro or lead carbonate treatment in vivo did not alter the uptake of ⁴⁵Ca by brain significantly. Release of ⁴⁵Ca by brain slices was inhibited by pretreatment of the tissues with Pb and by addition of either ouabain or sodium azide to the incubation medium. Retention of ⁴⁵Ca at 5 minutes was increased 75% in animals treated in vivo with Pb carbonate, 69% in tissues incubated in vitro with ouabain and 48% with sodium azide. However, none of these treatments altered ⁴⁵Ca perfused through the cerebroventricular system in animals receiving 165 mg of lead carbonate daily for 5 days, who showed no significant difference compared to controls. Results favor a specific effect of inorganic lead on the mediated efflux of Ca from the incubated brain slice. This effect in another example of lead/calcium interactions in the nervous system. 23 references. (Author abstract modified)

002448 Kincaid-Smith, P.; Burrows, G. D.; Davies, B. M.; Holwill, B.; Walter, M.; Walker, R. G. Dept. of Nephrology, Royal Melbourne Hospital, Victoria 3050, Australia **Renal-biopsy findings in lithium and prelithium patients.** *Lancet.* No. 8144:700-701, 1979.

A comparative histological survey of renal biopsy material from age matched lithium, prelithium, and donor kidneys used for cadaver transplantation, which documents the existence of a previously reported unique specific tubular lesion caused by lithium, is described in a letter to the editor. The specific tubular lesion is found in the cortical and medullary collecting ducts and distal convoluted tubules. It develops very soon after lithium is started and is absent in kidney sampled a year after lithium has been stopped. Significant differences which were found in the histological changes between the nine donor kidneys and both the lithium (n=16) and prelithium (n=9) patients, are described. 5 references.

002449 Kuhnley, E. John; Granoff, Abbot L. Granoff: 316 Citizens Trust Bldg., 6330 Newtown Road, Norfolk, VA 23502 **Exfoliative dermatitis during lithium treatment.** *American Journal of Psychiatry.* 136(10):1340-1341, 1979

A case is which a patient receiving lithium developed a pruritic maculopapular rash and then exfoliative dermatitis is reported. A 16-year-old boy was referred for evaluation due to periods of depression alternating with periods of hyperactivity. The patient was diagnosed as having manic depressive illness and was started on 900mg/day of lithium carbonate. When the lithium was discontinued the patient's skin cleared spontaneously. Readministration of lithium produced an immediate recurrence.

It is concluded that in addition to maculopapular rashes, exfoliative dermatitis may be added to the list of cutaneous side-effects of lithium administration. 7 references.

002450 Kumar, Bharat B. Mt. Pleasant Regional Center for Developmental Disabilities, 1400 West Pickard, Mt. Pleasant, MI 48858. An unusual case of akathisia. *American Journal of Psychiatry*. 136(8):1088, 1979.

A case study is reported of a mentally retarded institutionalized man who had akathisia, a side-effect of antipsychotic drug therapy. Because he could not verbalize his symptoms, his episodic manifestations continued. Administration of an antiparkinsonian drug eliminated the episodes of akathisia. 4 references.

002451 Lehmann, H. E. Dept. of Psychopharmacology, Research and Training Building, McGill University, 1033 Pine Avenue West, Montreal, Quebec, Canada H3A 1A1. Negative aspects of psychotherapeutic drug treatment. *Progress in Neuro-Psychopharmacology*. 3(1-3):223-229, 1979.

Seven negative aspects of psychotherapeutic drug treatment are reviewed. The seven categories of negative effects of psychotropic substances are: 1) physical symptoms, e.g. headache, dry mouth, dizziness; 2) somatic complications, i.e., conditions which seriously impair the patient's health, e.g. cholestatic jaundice or tardive dyskinesia; 3) behavioral toxicity, i.e. noxious modifications of the patient's behavior as the result of the drug's action, e.g. drug dependence, psychomotor retardation; 4) compliance problems, i.e. irregular or unreliable adherence to the prescribed drug regimen by the patient; 5) restriction of the patient's learning capacity which may represent an obstacle to the application of other treatment modalities, e.g. behavior modification, or to the patient's social readaptation; 6) psychodynamic interference with psychotherapy, e.g. by diminishing the patient's motivation to pursue this type of treatment or by disturbing the structure of his defenses; and 7) reducing the physicians' therapeutic efficacy if he relies exclusively on psychotropic agents. 22 references. (Author abstract modified)

002452 Lesser, Ronald P.; Fahn, Stanley; Snider, Stuart R.; Cote, Lucien J.; Isgreen, William P.; Barrett, Robert E. Fahn: Neurological Institute, 710 West 168th Street, New York, NY 10032. Analysis of the clinical problems in parkinsonism and the complications of long-term levodopa therapy. *Neurology*. 29(9):1253-1260, 1979.

Clinical problems in parkinsonism and the complications of long-term levodopa therapy were investigated via evaluation of current status of 131 patients with idiopathic parkinsonism who were receiving levodopa therapy. Residual parkinsonian symptoms and signs were tabulated, as were the adverse effects from medication. Response to therapy was correlated with duration of the disease and with duration of treatment. Patients with on/off or wearing off effects were likely to have been treated for 4 years or longer. Patients treated with levodopa for 4 to 8 years were significantly more impaired with parkinsonism than patients treated for 0 to 3 years, even when patients were matched for total duration of disease. These data suggest that the deterioration of responsiveness after several years of levodopa therapy may be due to the therapy itself. These findings support the concept that utilization of levodopa therapy should be delayed until a patient becomes significantly impaired in occupational or social situations. 33 references. (Author abstract modified)

002453 Liebowitz, Michael R.; McGrath, Patrick J.; Bush, Sydney C. New York State Psychiatric Institute, 722 W. 168th St., New York, NY 10032. Mania occurring during treatment for depersonalization: a report of two cases. *Journal of Clinical Psychiatry*. 41(1):33-34, 1980.

Two cases in which young female patients with severe depersonalization became floridly manic in response to stimulant and antidepressant drug treatment are reported. It is suggested that both patients suffered bipolar affective disorder and that both presented with depressive episodes characterized by prominent depersonalization. Alternatives to this hypothesis are suggested, but one patient's total symptom remission and good response to lithium maintenance, and the second patient's clinical course, which involved a definite, although abbreviated second cycle of depression and mania, incline toward diagnoses of bipolar affective disorder. 9 references. (Author abstract modified)

002454 Lipscomb, Patricia A. Dept. of Psychiatry and Behavioral Sciences RP-10, University of Washington School of Medicine, Seattle, WA 98195. Cardiovascular side effects of phenothiazines and tricyclic antidepressants: a review with precautionary measures. *Postgraduate Medicine*. 67(3):189-192, 195-196, 1980.

The cardiovascular side-effects of therapeutic doses of phenothiazines and tricyclic antidepressants are reviewed and the need for caution in minimizing complications is suggested. Lethal arrhythmias can occur with such drugs, although the instances are rare, and hypotensive and EEG side-effects have also been noted. Most disturbing is the fact that major and possibly fatal arrhythmias can occur in young adults without antecedent heart disease, especially with thioridazine. Physicians should institute individualized treatment programs that include treatment with these psychotropic compounds and should carefully monitor patient response. 26 references.

002455 Ludwig, Arnold M. Department of Psychiatry, University of Kentucky College of Medicine, Lexington, KY. Anxiety and substance abuse. *Psychiatric Annals*. 9(10):19-21, 25-26, 1979.

The relationship between anxiety and substance abuse is explored. Clinical signs and symptoms of anxiety attacks, conditions in which anxiety may be present, and some nondepressant agents associated with anxiety are reviewed in table format. Primary anxiety preceding drug use, anxiety secondary to drug intoxication, anxiety secondary to physical dependence, and anxiety and relapse to drug abuse are discussed. It is suggested that when substance abuse represents a consequence of anxiety initial treatment must be directed toward the superimposed problems and complications of the drug dependency since these represent the most immediate danger. Once the patient is detoxified, more definitive treatment is recommended to control or eliminate the basic anxiety underlying the use of these drugs. 3 references.

002456 MacLeod, Norman; Kratochvil, C. H. Upjohn Ltd., Crawley, West Sussex RH10 2NJ, England. Behavioural reactions to triazolam. *Lancet*. No. 8143:638-639, 1979.

Results regarding the behavioral side-effects of the hypnotic triazolam are reviewed. It is asserted that a report of adverse effects such as depression, nightmares, hallucinations, and confusion contradicts data from a large number of other studies. Results based on 50 million patient nights of triazolam therapy indicate a low incidence of adverse reactions. The weight of evidence appears to refute findings of a clustering of symptoms. It is concluded that the adverse findings are based on subjective evaluations and cannot be accepted as decisive.

002457 Magorien, Raymond D.; Jewell, Gregory M.; Schaal, Stephen F.; Leier, Carl V. Division of Cardiology, Ohio State University Hospitals, 653 Means Hall, 466 West Tenth Ave., Columbus, OH 43210. Electrophysiologic studies of perphenazine and protriptyline in a patient with psychotropic drug-induced ventricular fibrillation. *American Journal of Medicine*. 67(2):353-357, 1979.

The case of 51-year-old woman who sustained ventricular fibrillation while receiving perphenazine and protriptyline is described. After successful resuscitation and clinical stabilization, cardiac electrophysiologic studies were performed before and after the administration of each of these medications. Perphenazine widened the ventricular echo zone and facilitated induction of short salvoes of ventricular tachycardia. Protriptyline also widened the ventricular echo zone and allowed easy induction of long runs of ventricular tachycardia. Both psychotropic agents increased the incidence of ventricular dysrhythmias in this patient. It is suggested that the electrophysiologic study is a useful technique in determining the interaction between psychotropic drugs and life threatening arrhythmias; it may provide a means of identifying the patients with cardiac disease in whom administration of these agents may be fatal. 20 references. (Author abstract modified)

002458 McLain, L. William, Jr.; Martin, J. True; Allen, Joseph H. Dept. of Neurology, University of Minnesota, Box 295 Mayo, 420 Delaware St. SE, Minneapolis, MN 55455 **Cerebellar degeneration due to chronic phenytoin therapy.** *Annals of Neurology*. 7(1):18-23, 1980.

The case histories of five patients who developed cerebellar degeneration while being treated with phenytoin are presented. All had high plasma levels of the drug, and none was having seizures of a type that could have caused systemic hypoxia at the time the cerebellar syndrome appeared. Cerebellar degeneration was confirmed by the finding of atrophy on CT scan and by persistence of cerebellar signs when plasma phenytoin levels were decreased. It is suggested that chronic phenytoin therapy can cause cerebellar degeneration. 37 references. (Author abstract modified)

002459 Monks, Anne; Richens, Alan. Richens: Clinical Pharmacology Unit, Institute of Neurology, Queen Square, London WC1N 3BG, England **Effect of single doses of sodium valproate on serum phenytoin levels and protein binding in epileptic patients.** *Clinical Pharmacology and Therapeutics*. 27(1):89-95, 1980.

The effect of single doses of sodium valproate on phenytoin steady-state serum concentration and protein binding was examined in patients with chronic epilepsy stabilized on phenytoin. Results showed that total serum phenytoin levels may fall when sodium valproate is added to therapy. This may lead to an increase in dose under the mistaken belief that the effect of the drug has been reduced, and phenytoin intoxication may result. 12 references. (Author abstract modified)

002460 Montouris, Georgia D.; Fenichel, Gerald M.; McLain, L. William, Jr. Fenichel: Dept. of Neurology, Vanderbilt University School of Medicine, Nashville, TN 37232 **The pregnant epileptic: a review and recommendations.** *Archives of Neurology*. 36(10):601-603, 1979.

Literature concerning the effect of pregnancy on epilepsy is reviewed. Studies indicate that the major concerns of the epileptic patient are loss of seizure control and the teratogenic effects of antiepileptic drugs on the fetus. Loss of seizure control is usually caused by a progressive decline of antiepileptic plasma levels throughout pregnancy. This decline can be prevented by monthly dose adjustments based on plasma level determinations. Although infant malformations are a more prevalent outcome of pregnancies of epileptics than of nonepileptics, the role of antiepileptic drugs in teratogenicity is not fully established. Only trimethadione has been convincingly linked to fetal malformation. Recommendations for the management of epilepsy in pregnancy are made. 70 references. (Author abstract modified)

002461 Nakane, Yoshitomi. Dept. of Neuropsychiatry, Nagasaki University School of Medicine, Nagasaki, Japan **Congenital malformation among infants of epileptic mothers treated during pregnancy -- the report of a collaborative study group in Japan.** *Folia Psychiatrica et Neurologica Japonica*. 33(3):363-369, 1979.

The report of a nationwide research effort investigating congenital malformation among infants of epileptic mothers treated during pregnancy with anticonvulsant drugs is described. Records of 902 pregnant women treated at 11 Japanese institutions were analyzed. Ss were divided into a treated group, a nontreated group, and a group in which medication history during pregnancy was not known. The malformation rates among live births of the first and the second groups were 11.5% and 2.3%, respectively; however, it is estimated that the rate would have been 6.75% among the treated group if trimethadione treatment had been avoided. The effects of maternal background and antiepileptic treatment were analyzed fully in connection with the possibility of congenital malformation. 10 references. (Author abstract modified)

002462 Nasrallah, Henry A. Psychiatry Service, VA Medical Center, Iowa City, IA 52240 **Neuroleptic plasma levels and tardive dyskinesia: a possible link?** *Schizophrenia Bulletin*. 6(1):4-7, 1980.

The hypothesis that the onset of tardive dyskinesia in chronically medicated schizophrenic patients may be related to a gradual decline in neuroleptic plasma concentration after years of treatment, probably due to increased metabolism of the drug as well as other factors in chronic neuroleptic treatment that may result in lowering of plasma concentrations is examined and supported. The symptoms are usually suppressed by increasing the neuroleptic dose which would result in higher plasma drug concentrations. The decline in neuroleptic plasma levels that gradually occurs with chronic daily drug intake is probably due to increased metabolism, and can be exacerbated by drug holidays, anticholinergic drugs, once a day dosage, erratic compliance, and depot neuroleptics, all of which can produce fluctuating blood levels. There may be a critical plasma concentration of neuroleptics corresponding to adequate DA receptor blockade below which a withdrawal hypersensitivity of DA receptors occurs, and this possibility merits study. 26 references. (Author abstract modified)

002463 Nery, Luiz Eduardo; Homs, Luiz; Godoy-Fernandes, Ana Luiza; Lopes-Dos-Santos, Manuel; Ratto, Octavio Ribeiro. Disciplina de Pneumologia do Departamento de Medicina da Escola Paulista de Medicina, Rua Botucatu 720, 04023 Sao Paulo, SP, Brazil **Acute respiratory failure associated with administration of central nervous system depressant drugs.** *Insuficiencia respiratoria aguda asociada a ingestao de drogas depressoras do sistema nervoso central.* *Arquivos de Neuro-Psiquiatria*. 37(3):217-229, 1979.

Clinical aspects, complications, and lung function impairment of 20 patients with poisoning by central nervous system depressant drugs were studied. Barbiturates, the most common drugs, were used at least in 60% of the cases, either alone or in combination with sedatives and tranquilizers. In 55% of the patients, the amount of the drug ingested could not be measured. In 60% of the cases, the period of time between drug ingestion by the patients and their admission to the hospital was unknown. On admission, all patients were in varying degrees of comas. Lung function was worse and complications were more frequent the deeper the coma. Whenever a cardiovascular collapse was present, there was also a high mortality rate. The importance of a followup of these patients in intensive care units, mainly with cardiovascular and ventilatory support, is emphasized. 19 references. (Journal abstract modified)

002464 Neu, Carlos; Manschreck, Theo C.; Flocks, Jay M. 300 Mount Auburn Street, Suite 410, Cambridge, MA 02138 **Renal damage associated with long term use of lithium carbonate.** *Journal of Clinical Psychiatry.* 40(11):460-463, 1979.

Two cases of renal damage associated with long-term lithium carbonate treatment are reported. In case 1, the patient was maintained on lithium carbonate for a period of 9 years for the treatment of manic-depressive illness. On admission to hospital, his lithium level was 2.2 mEq/L. Two days after admission, the patient was confused, disoriented, his social behavior deteriorated, and his speech became unintelligible. The patient's condition was diagnosed as lithium nephrotoxicity due to irreversible interstitial fibrosis, and polydipsia and polyuria due to nephrogenic diabetes insipidus. Although lithium was discontinued, abnormal renal function remained unchanged and psychiatric status was moderately impaired despite antipsychotic medication. In case 2, renal damage was found in a 29-year-old male treated for manic-depressive disorder since 1970 with psychotherapy, lithium, tricyclics, and intermittent antipsychotics. Following admission in 1978, testing revealed chronic interstitial nephritis secondary to chronic lithium treatment. Lithium was discontinued and the patient remains hospitalized in a severe state of psychiatric impairment. 14 references. (Author abstract modified)

002465 no author. no address **Tardive dyskinesia.** *British Medical Journal.* No. 6201:1313, 1979.

The problem of tardive dyskinesia is discussed. Tardive dyskinesia, a side-effect of neuroleptic drugs, is characterized and various courses of treatment are reviewed, although it is noted that none is particularly effective. The best hope or prevention of the syndrome is seen as care and discrimination in the use of neuroleptics. In the long run, it is suggested, the answer must lie in the development of a new class of neuroleptic drugs that will control schizophrenia without producing tardive dyskinesia. 7 references.

002466 no author. no address **Lithium and the kidney: grounds for cautious optimism.** *Lancet.* No. 8151:1056-1057, 1979.

Recent research studies concerning the putative nephrotoxicity of long-term lithium therapy for affective illness are reviewed. Issues discussed include: affective disorder patients as control Ss for studies of lithium nephrotoxicity, the nephrotoxicity of neuroleptic drugs, and the risk of lithium nephropathy in the absence of lithium toxicity. It is noted that the putative toxicological effect of lithium on the kidneys must not be confused with the pharmacological nephrogenic diabetes insipidus it gives rise to, whereby the sensitivity of action of antidiuretic hormone on the distal convoluted tubule is blunted. It is concluded that the risk of lithium nephropathy in the absence of lithium toxicity is small. 18 references.

002467 no author. no address **Lithium nephropathy.** *Lancet.* No. 8143:619-620, 1979.

Lithium side-effects involving renal function are described. The most common effect is initial sodium diuresis followed by a few weeks of mild polyuria and polydipsia. About 10% of lithium patients have impairment of renal concentrating ability which may persist or recur. Occasionally, frank nephrogenic diabetes insipidus may occur. The mechanism of lithium generated nephropathy has not been determined. There have been few reports of renal tubular damage in animals exposed to lithium. Isolated cases of renal failure associated with acute lithium intoxication have been reported. Studies have been conducted of nephropathy in lithium patients is not high, psychiatrists should remain aware of lithium's narrow margin of safety. 20 references.

002468 Pedersen, Robert Smith; Heath, Andrew; Wickstrom, Ingemar; Ahlmen, Jarl; Trafford, Anthony; Sharpstone, Paul; O'Neal, Hugh. Dept. of Nephrology, Aalborg Hospital (South Section), DK-9100 Aalborg, Denmark **Haemoperfusion in tricyclic antidepressant poisoning.** *Lancet.* No. 8160:154-155, 1980.

In three letters to the editor, hemoperfusion in tricyclic antidepressant poisoning is discussed. Case histories in which poisoning from tricyclic antidepressants, mushrooms, chloral hydrate, and digitoxin were treated with hemoperfusion are presented. The prompt clinical improvement of these patients with ventricular arrhythmias and grade IV comas suggest that a large distribution volume of the drug is not the only factor that determines the efficacy of hemoperfusion. With the 'Amberlite' hemoperfusion system, an effective clearance of the drug correlated to an improved clinical condition, suggesting that it is the rate of movement between the different compartments which determines how much of the drug can be removed. 12 references.

002469 Peterson, Linda Gay; Popkin, Michael K. Department of Psychiatry, University Hospital, Box 393, Mayo Memorial Building, Minneapolis, MN 55455 **Neuropsychiatric effects of chemotherapeutic agents for cancer.** *Psychosomatics.* 21(2):141-143, 146-147, 151-153, 1980.

The literature on the psychiatric effects of the major groups of cancer chemotherapy agents, exclusive of hormones, is reviewed. It was found that CNS complications from such therapy range from 5% to 86% for different classes of drugs. However, patients receiving cancer chemotherapy are rarely given a systematic psychiatric evaluation. Psychiatric sequelae are seldom noted in the absence of neurologic disturbances. Organic mental disorders and affective disturbances are most frequently observed, while acute psychotic reactions are very uncommon. Most changes appear reversible, with the exception of a significant incidence of chronic CNS effects following high dose intravenous or intrathecal methotrexate therapy. 100 references. (Author abstract modified)

002470 Pohl, Robert B.; Berchou, Richard; Gupta, Bal K. Department of Psychiatry, School of Medicine, Wayne State University, Detroit, MI **Lithium-induced hypothyroidism and thyroiditis.** *Biological Psychology.* 14(5):835-837, 1979.

The evidence for the hypothesis that patients with a preexisting thyroiditis may be particularly susceptible to a rapid onset of lithium-induced hypothyroidism is reviewed. A case report illustrating this phenomenon is presented. It is recommended that further prospective studies are needed utilizing pretreatment antithyroid antibody levels to elucidate the role of thyroiditis in lithium-induced hypothyroidism. 8 references. (Author abstract modified)

002471 Rabin, E. Z.; Garston, R. G.; Weir, R. V.; Posen, G. A. Division of Nephrology, Ottawa Civic Hospital, 1053 Carling Avenue, Ottawa, Ontario K1Y 4E9, Canada **Persistent nephrogenic diabetes insipidus associated with long-term lithium carbonate treatment.** *Canadian Medical Association Journal.* 121(2):194-195, 197-198, 1979.

The case history of a 44-year-old woman with nephrogenic diabetes insipidus that had developed 6 years after the beginning of lithium therapy and persisting 4 years after the termination of lithium treatment is reported. Discontinuation of the drug failed to correct the initial complaints of polyuria and polydipsia, and it appeared that the patient had permanent diabetes insipidus with resistance to antidiuretic hormones. She also had a depressed glomerular filtration rate and renal interstitial fibrosis, particularly in the medulla. A relation is suggested between the ingestion of lithium and the patient's condition for the following

reasons: 1) lithium therapy is known to induce a reversible defect identical to this one, 2) lithium therapy has been shown to be associated with renal fibrotic lesions, 3) the interstitial fibrosis was more prominent in the areas of the kidney known to accumulate lithium, 4) no other drug or disease could be found to account for the diabetes with resistance to antidiuretic hormone, and 5) two previous cases have been reported in which permanent diabetes insipidus appeared to be induced by lithium therapy. 7 references.

002472 Rapoport, J.; Chaimovitz, C.; Alroy, G. G.; Better, O. S. Dept. of Nephrology, Rambam University Hospital, Haifa, Israel **Lithium-induced nephrogenic diabetes insipidus: studies of tubular function and pathogenesis.** *Israel Journal of Medical Sciences.* 15(9):765-771, 1979.

A patient is described with lithium-induced nephrogenic diabetes insipidus in whom detailed investigations of distal tubular function were performed. Clearance of free water during water diuresis was augmented and reabsorption of free water during high solute clearance was impaired. Acidification of the urine following ammonium chloride loading was abnormal and was corrected by sodium sulfate infusion. Indomethacin, an inhibitor of prostaglandin synthesis, caused a partial reversal of the nephrogenic diabetes insipidus, suggesting that the primary cellular action of lithium may be to inhibit the formation of cyclic AMP in the collecting duct cell, although a direct action of indomethacin in increasing solutes in the renal medulla cannot be ruled out. It is possible that lithium-induced polyuria is partially due to an enhancement by lithium of renal prostaglandin action. references. (Author abstract modified)

002473 Rapp, Morton S. Affective Disorder Clinic, Rm. G745, Sunnybrook Hospital, 2075 Bayview Ave., Toronto, Ontario, M4N 3M5, Canada **Two cases of ejaculatory impairment related to phenelzine.** *American Journal of Psychiatry.* 136(9):1200-1201, 1979.

Two cases of ejaculatory impairment, occurring in a relatively short time, following adequate doses of phenelzine, are reported. In both cases ejaculatory impairment followed an increase in daily dosage of phenelzine from 60mg to 75mg. When dosage was returned to 60mg, a low level and somewhat ineffective dosage, the side-effects disappeared. Since these two cases occurred in a practice where phenelzine is employed only about 12 times a year, it is suggested that there may be a high incidence of ejaculatory complaints in patients taking the recommended dose of phenelzine. 2 references.

002474 Rebec, G. V.; Bashore, T. R.; Zimmerman, K. S.; Alloway, K. D. Dept. of Psychology, Indiana University, Bloomington, IN 47405 **Neostriatal and mesolimbic neurons: dose-dependent effects of clozapine.** *Neuropharmacology.* 19(3):281-288, 1980.

To determine whether clozapine, an antipsychotic drug devoid of extrapyramidal side-effects, acts preferentially on neurons in the nucleus accumbens rather than in the neostriatum, an analysis of clozapine-induced changes in spontaneous neuronal activity was performed on locally anaesthetized, immobilized rats. In both sites intraperitoneal administration of 10, 20, or 80mg/kg doses produced a comparable dose dependent increase in neuronal activity. Haloperidol at a dose that typically elicits extrapyramidal side-effects also increased the firing rate of neurons in the neostriatum and nucleus accumbens. Haloperidol, however, produced a greater effect on neuronal activity in the neostriatum during the first 15 min after injection, whereas 80mg/kg clozapine was more effective during this period in the nucleus accumbens. The overall results suggest that the lack of extrapyramidal side-effects associated with clozapine cannot be

simply explained by a selective action of this drug on neurons in the nucleus accumbens. 56 references. Author abstract modified)

002475 Rhoads, John M.; Lowell, Seth H.; Hedgepeth, Emmett M. Duke University Medical Center, Durham, NC 27710 **Hoarseness and aphonia as a side effect of tricyclic antidepressants.** *American Journal of Psychiatry.* 136(12):1599, 1979.

A case of hoarseness and aphonia as side-effects of tricyclic antidepressants is described. A 50-year-old man was treated for neurotic depression with doxepin at 75mg/day. He had reported hoarseness, and an examination revealed mild diffuse throat inflammation but no gross pathology. The doxepin was discontinued and 100mg/day of nortriptyline was administered upon admission to the hospital. The patient complained of a sore throat and increasing hoarseness, and was unable to speak by the sixth day after admission. The medication was discontinued and the symptoms gradually disappeared. He was later treated for depression with tranlycypromine sulfate with no side-effects. It is suggested that his heavy smoking habit contributed to this side-effect.

002476 Roizin, L. Dept. of Neuropathology and Neurotoxicology, NYS Psychiatric Institute, 722 East 168th Street, New York, NY 10032 **The relevance of the structural co-factor (chemogenic lesion) in adverse and toxic reactions of neuropsychotropic agents.** *Progress in Neuro-Psychopharmacology.* 3(1-3):245-257, 1979.

The relevance of the structural cofactor (chemogenic lesion) in adverse and toxic reactions of neuropsychotropic agents is discussed. Multidisciplinary methods in human and experimental investigations have revealed that neuropsychotropic agents display multiple neuronal and extraneural targets or bioreceptors. The adverse and toxic reactions are conceived of as the expression of a reversible or irreversible chemogenic lesion resulting from the molecular interactions among the chemical agents and the morphochemical correlates of the organism at any level of the structural organization. In pathogenic terms, this chemogenic lesion appears as a pathochemical condition or a dynamic state of interaction chemical and biological mechanisms rather than a single cause. 41 references. (Author abstract modified)

002477 Ruuskanen, I.; Kilpelainen, H. O.; Riekkinen, P. J. Riekkinen: Dept. of Neurology, University of Kuopio, P.O.B. 138, SF-70101 Kuopio 10, Finland **Side effects of sodium valproate during long-term treatment in epilepsy.** *Acta Neurologica Scandinavica.* 60(2):125-128, 1979.

Side-effects of sodium valproate during long-term treatment was evaluated retrospectively in 55 patients suffering from refractory epilepsy. The side-effects discovered in the study were slight and transient. In three of the 55 patients, CNS side-effects were noticed. Gastrointestinal symptoms were uncommon. One patient suffered from loss of hair which could have been attributed to sodium valproate. Severe side-effects such as abnormal blood counts or organic damage were not discovered. The frequency of side-effects was similar to those already reported in the literature except for gastrointestinal symptoms which were more frequent than previously reported. No direct correlation could be established between the serum concentration of sodium valproate and the side-effects. 11 references. (Author abstract modified)

002478 Sackellares, J. Chris; Lee, Soo Ik; Dreifuss, F. E. Dept. of Neurology, School of Medicine, University of Virginia, Charlottesville, VA 22908 **Stupor following administration of valproic acid to patients receiving other antiepileptic drugs.** *Epilepsia.* 20(6):697-703, 1979.

Four cases of stupor, an unusual complication following the addition of valproic acid to other antiepileptic drugs, are reported. Stupor occurred acutely in three patients and insidiously in the fourth. Neither toxic levels of valproate nor significant elevations in blood levels of the other drugs occurred in the cases of acute toxicity; in the fourth patient, stupor occurred concomitantly with a rise in the phenobarbital level. EEGs of all four patients revealed generalized high amplitude rhythmic bisynchronous delta activity. Recovery occurred following discontinuation of valproic acid or other antiepileptic drugs. It is suggested that stupor may occur as a result of drug interactions after the addition of valproic acid to other antiepileptic drugs. 13 references. (Author abstract modified)

002479 Santos, Alberto B., Jr.; McCurdy, Layton. Psychiatry Education Branch, NIMH, 5600 Fishers Lane, Room 8C06, Rockville, MD 20857 **Delirium after abrupt withdrawal from doxepin: case report.** *American Journal of Psychiatry.* 137(2):239-240, 1980.

Case data are presented from a depressed patient who developed delirium after doxepin therapy was discontinued abruptly. The biochemical mechanisms involved in this reaction were not clear and a delirious reaction upon doxepin withdrawal seems paradoxical. The concomitant administration of disulfiram was a complicating factor. Both drugs modify metabolic balance in one or more neurotransmitter systems, and the tentative results support a biochemical hypothesis. 5 references.

002480 Seino, Masakazu; Miyakoshi, Masako. National Epilepsy Center, Shizuoka Higashi Hospital, Shizuoka, Japan **Teratogenic risks of antiepileptic drugs in respect to the type of epilepsy.** *Folia Psychiatrica et Neurologica Japonica.* 33(3):379-385, 1979.

The teratogenic risks of anticonvulsant drugs were investigated as a function of the type of epilepsy suffered by the mothers. Data from 428 females of childbearing age suffering from various types of epilepsy were analyzed. Results indicate that mothers with epilepsy receiving antiepileptic drugs during pregnancy had unequivocally more frequent malformations among their offspring than mothers who were not treated. Among mothers who were treated during pregnancy, polypharmacy and overdose were associated with increased incidence of malformed children. This undesirable regimen was most common for mothers with secondary generalized epilepsy or complex partial seizures. 16 references.

002481 Shabry, Fryderyka; Wolk, Joel A. Wolk: Brookdale Hospital Medical Center, Brooklyn, NY 11212 **Granulocytopenia in children after phenothiazine therapy.** *American Journal of Psychiatry.* 137(3):374-375, 1980.

The incidence of granulocytopenia, the most common adverse hematological drug reaction, was examined in 10 children (nine Black, one Puerto Rican) in a partial hospitalization program who were treated with phenothiazines during a 1 year study period. Psychiatric diagnosis included childhood schizophrenia (n=5), latent schizophrenia (n=3), severe mental retardation with autistic features (n=1), and behavior disorder of childhood/unsocialized aggressive reaction (n=1). Granulocytopenia occurred in only one patient; 5 months after thioridazine was discontinued, his leukocyte and granulocyte counts returned to pretreatment levels. Findings highlight the need for hematologic evaluation of children receiving phenothiazine therapy. 7 references.

002482 Sironi, V. A.; Franzini, A.; Ravagnati, L.; Marossero, F. Istituto di Neurochirurgia dell'Università, Pad. Beretta, Ospedale Policlinico, Via F. Sforza 35, I-20122 Milano, Italy **Interictal acute psychoses in temporal lobe epilepsy during with-**

drawal of anticonvulsant therapy. *Journal of Neurology, Neurosurgery, and Psychiatry.* 42(8):724-730, 1979.

Acute interictal psychotic attacks during withdrawal of medication are described in two patients with temporal lobe epilepsy submitted to depth EEG study with a view to surgical treatment. The patients were on chronic treatment with clonazepam associated in one with phenobarbitone and in the other with phenobarbitone plus carbamazepine. The observations suggest that the acute withdrawal of clonazepam, the plasma levels of which were monitored, may play a part in producing psychotic attacks characterized by dysphoric manifestations, irritability, aggressiveness, anxiety, and hallucinations. These symptoms could be interpreted as a withdrawal syndrome. 23 references. (Author abstract)

002483 Stanley, Michael; Rotrosen, John; Lautin, Andrew; Wazer, David; Gershon, Samuel. Dept. of Psychiatry, New York University Medical Center, New York, NY 10016 **Tardive dyskinesia and metoclopramide.** *Lancet.* No. 8153:1190, 1979.

The chronic use of metoclopramide and its side-effects are examined. Interest in metoclopramide stems from the fact that it is active in nearly all systems which measure dopamine antagonism, yet is inactive in both of the currently used CNS dopamine receptor models. Preclinical findings indicate that chronic treatment with metoclopramide can produce behavioral supersensitivity, besides inducing an increase in dopamine receptor density. In patient trials with schizophrenics, metoclopramide was found to be an effective antipsychotic. The profile of metoclopramide is consistent with reports of extrapyramidal side-effects and tardive dyskinesia. It is concluded that tardive dyskinesia may be an unavoidable risk associated with all agents owing their antipsychotic activity to dopamine antagonism. 7 references.

002484 Stern, Stephen L.; Mendels, J. Depression Research Unit (151E), V.A. Medical Center, University and Woodland Avenues, Philadelphia, PA 19104 **Withdrawal symptoms during the course of imipramine therapy.** *Journal of Clinical Psychiatry.* 41(2):66-67, 1980.

Two cases in which withdrawal symptoms occurred during the course of imipramine therapy for depression, after the patients had failed to take a single daily dose of medication, are described. In both cases the patients had been on imipramine therapy for 2 weeks, experienced nausea after missing their once daily dosage, and experienced prompt remittance of symptoms after taking the medication. Similar withdrawal symptoms have been noted upon discontinuation of imipramine and its derivatives desipramine and chlorimipramine, but have not, with one exception, been reported in association with other tricyclics. 13 references. (Author abstract modified)

002485 Tanimura, Takashi. Dept. of Anatomy, Kinki University School of Medicine, Osaka, Japan **Evaluation of the teratogenicity of anticonvulsants.** *Folia Psychiatrica et Neurologica Japonica.* 33(3):371-377, 1979.

Issues concerning the evaluation of the teratogenicity of anticonvulsant drugs are discussed, and suggestions for evaluation and comparison of reports of teratogenicity of drugs are presented. Topics discussed include: problems in surveys of congenital malformations, problems in surveys of teratogenicity of chemicals, specific problems in evaluation of the teratogenicity of anticonvulsants, and the evaluation of animal studies on the teratogenicity of anticonvulsants. Since the etiological significance of anticonvulsants has not been established in humans, the following strategies are suggested: 1) systematic collection and detailed analysis of more human cases; 2) study on the role of epilepsy and treatment with multiple drugs; and 3) investigation

of the mechanism of teratogenesis, including comparative pharmacokinetic studies in animals and humans. 14 references. (Author abstract modified)

002486 Tepper, Stewart J.; Haas, Joanna F. Haas: Cornell Medical Center, 525 East 68th Street, New York, NY 10021 **Prevalence of tardive dyskinesia.** *Journal of Clinical Psychiatry.* 40(12):508-516, 1979.

Diagnostic criteria, objective scale and assessment, interobserver reliability, period of observation, and specific interhospital coordination were evaluated in 44 epidemiological studies of tardive dyskinesia. Studies which met these criteria were reviewed for data on class of neuroleptic, therapy, dose, duration, continuity of treatment, extrapyramidal toxicity, spontaneous dyskinesias, other drugs and treatment modalities, age, and sex. A higher prevalence of tardive dyskinesia has been consistently noted in the elderly and in females. No other predisposing factors for tardive dyskinesia have thus far been conclusively demonstrated. Prevalence of tardive dyskinesia is estimated at 24% to 56% in chronic neuroleptic users. 53 references. (Author abstract modified)

002487 Tyrer, P.; Alexander, M. S.; Regan, Adrienne; Lee, I. Mapperley Hospital, Nottingham NG3 6AA, England **An extrapyramidal syndrome after lithium therapy.** *British Journal of Psychiatry.* 136(February):191-194, 1980.

Case histories of two patients who developed an extrapyramidal syndrome after therapy with lithium carbonate are reported. Although the clinical features of this syndrome were indistinguishable from those of drug-induced parkinsonism, it was made worse by the antiparkinsonian drug, orphenadrine. These findings were reproduced later under laboratory conditions when extrapyramidal symptoms and physiological tremor were recorded before and after challenge doses of orphenadrine. This unwanted effect of lithium carbonate may be explained by selective blockade of dopamine receptors. 13 references. (Author abstract modified)

002488 Verebey, Karl; Mule, S. Joseph. New York State Alcoholism and Substance Abuse Services, Testing and Research Laboratory, 80 Hanson Place, Brooklyn, NY 11217 **Naltrexone and beta-naltrexol plasma levels in schizophrenic patients after large oral doses of naltrexone.** *Research Communications in Psychology, Psychiatry and Behavior.* 4(3):311-317, 1979.

The toxicity and side-effects of varying doses of naltrexone and its major metabolite, beta-naltrexol, were tested in schizophrenic patients to determine the margin of safety for naltrexone as an opiate antagonist. Naltrexone doses from 100 to 800mg/daily were given to 6 schizophrenic patients. The plasma levels of naltrexone and its major metabolite increased to very high levels without therapeutic improvement, toxicity or any undesirable side-effects. Two weeks after the discontinuation of the 800mg naltrexone dose, the plasma was free of both naltrexone and beta-naltrexol--indicating a rapid and efficient elimination of the drug. Since the proposed role of naltrexone is opiate antagonism in narcotic postaddicts, and effective heroin blocking doses for a 72 hour period are 100 to 200mg of naltrexone; the drug appears to possess a high margin of safety even when used at considerably higher doses. 14 references. (Author abstract modified)

002489 Vestergaard, P.; Amdisen, A.; Hansen, H. E.; Schou, M. Psychopharmacology Research Unit, Psychiatric Hospital, DK-8240 Risskov, Denmark **Lithium treatment and kidney function: a survey of 237 patients in long-term treatment.** *Acta Psychiatrica Scandinavica.* 60(5):504-520, 1979.

Kidney function was examined in 237 patients who were in lithium treatment as outpatients. The patients had been given lithium treatment for 0.5 to 17 years. The mean lithium dosage was 33 mmol/day and the mean 12 hour serum lithium concentration was 0.85 mmol/l. Creatinine clearances, serum creatinine concentrations, and urine volumes were subjected to multiple regression analysis with various clinical predictor variables. Affection of glomerular filtration rate was only moderate and progressed slowly. The data indicate that the risk of renal insufficiency and terminal azotemia is remote even when lithium is given for many years. A large number of the patients had altered water excretion with polyuria or lowered urine concentrating ability or both. Due to the extra fluid loss these patients are apt to develop dehydration, and they may then be in danger of lithium poisoning. It is hypothesized that lithium-induced changes of kidney function may become less frequent and less pronounced if patients are maintained at serum lithium levels somewhat lower than those in the group studied. Careful monitoring of serum lithium levels, regular control of kidney function, and extra caution when physical illness or additional drug treatment may lead to disturbance of fluid and electrolyte balance are recommended. 25 references. (Author abstract modified)

002490 Vestergaard, Per; Hansen, Hans E. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Psychiatric Hospital, DK-8240 Risskov, Denmark **Assessment of renal concentrating ability in lithium-treated patients: comparison of long-term dehydration with administration of a vasopressin analogue.** *Acta Psychiatrica Scandinavica.* 61(2):152-156, 1980.

In patients given long-term treatment with lithium maximum urine osmolality was measured after 26 hours of dehydration and after intranasal administration of desamino-8-D-arginine vasopressin (DDAVP). A high correlation was found between the results of the two tests suggesting that the DDAVP test is a suitable method of assessing renal concentrating ability in lithium treated patients. The DDAVP test is recommended to avoid the inconveniences and the risk of excess dehydration connected with the long-term thirst test. 10 references. (Author abstract modified)

002491 Wagner, George C.; Ricaurte, George A.; Seiden, Lewis S.; Schuster, Charles R.; Miller, Richard J.; Westley, John. Seiden: Dept. of Biopsychology, University of Chicago, Chicago, IL 60637 **Long-lasting depletions of striatal dopamine and loss of dopamine uptake sites following repeated administration of methamphetamine.** *Brain Research.* 181(1):151-160, 1980.

Repeated administration of high doses of methamphetamine to male Sprague-Dawley rats produced long-term decreases in levels of dopamine (DA) and in the number of DA uptake sites in the striatum. These effects were dose related, did not appear to be due to the continued presence of drug in the striatal tissue, and were not accompanied by supersensitivity. The long-lasting depletions induced by methamphetamine were selective for striatal DA neurons; norepinephrine levels showed no long-term changes in response to methamphetamine in any of the regions examined. 16 references. (Author abstract modified)

002492 Wasik, August; Kiejna, Andrzej; Puchala, Grazyna; Brys, Jozef. Klinika Psychiatryczna AM, ul. Kraszewskiego 25, 50-229 Wrocław, Poland **Complications and side-effects of lithium therapy described in materials of the Psychiatric Clinic in Wrocław.** *Powiklania i objawy uboczne terapii litem w materiale Kliniki Psychiatrycznej we Wrocławiu.* *Psychiatria Polska.* 13(2):103-109, 1979.

Complications and side-effects of lithium administered to 47 mental patients suffering from manic-depressive psychosis were

studied. It was found that lithium inhibits the functions of the thyroid gland and sometimes causes hypofunction of the gland or neutral goiter. Other side-effects on other organs were found, mostly those of a neurological nature, such as tremulousness and myoclonia. Psychological symptoms, including a decrease in general activity and reduced cognitive ability, also were observed. It is suggested that patients who qualify for lithium treatment should be given an endocrinological test to avoid dysfunction of the thyroid gland. If symptoms of thyroid dysfunction appear, the patients should be treated with thyroid hormones. 14 references. (Journal abstract modified)

002493 Wendt, Roselyn L. Oakridge Gardens Nursing Center, Menasha, WI 54952 *American Journal of Nursing*. 79(5):949, 1979.

Experiences of a nurse on psychotropic drugs are recounted. Psychotropic drugs were prescribed after hospitalization for severe depression following a suicide attempt, and she continued taking the drugs prescribed for maintenance for 2 years following hospitalization. While on medication, she was mostly oblivious to what went on around her, was unable to fully enjoy the good or cope with the bad, and was never fully awake. Other side-effects included spasms in the calves of her legs, difficulty speaking clearly, dry mouth, nasal congestion, and weight gain. The medication also stimulated lactation and caused a loss of libido. The difficulties she faced with job applications and other situations are briefly reported.

002494 Wilner, Keith D.; Butler, Ian J.; Seifert, William, E. Jr.; Clement-Cormier, Yvonne C. Dept. of Pharmacology, University of Texas Medical School, Houston, TX 77030 *Biochemical alterations of dopamine receptor responses following chronic L-dopa therapy*. *Biochemical Pharmacology*. 29(5):701-706, 1980.

The effects of chronic L-dopa treatment on rat striatal adenylyl cyclase and dopamine receptor binding activities were studied using an oral dose of Sinemet (20mg L-dopa and 25mg carbidopa). The calculated average daily oral intake of L-dopa was 150mg/rat. A four fold increase in the EC50 for dopamine on adenylyl cyclase activity in homogenates of the caudate nucleus was observed in the oral drug treated group with no change in the maximal level of enzyme activity. Binding studies using (3H)spiroperidol, a dopamine receptor antagonist, revealed a decrease in the dissociation constant from 0.26nM in the control group to 0.069nM in the oral drug treated group. In addition, the Bmax for (3H)spiroperidol specific binding in the animals receiving oral L-dopa increased by 300 fmole/mg over that observed in the control group. Dopamine sensitive adenylyl cyclase and binding activities in animals receiving a lower dose of L-dopa alone, given intraperitoneally twice daily, were determined to be similar to control values. Analysis of the cerebrospinal fluid biogenic amine metabolites, homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA) and 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG), by gas chromatography/mass spectrometry revealed a 13 fold increase in HVA following oral L-dopa and a 44% increase in MHPG levels. These data, which demonstrate an increased number of dopamine binding sites following long-term L-dopa therapy, are consistent with demonstrations of behavioral hypersensitivity in animals undergoing this particular drug treatment. 45 references. (Author abstract)

002495 Wilson, J. T.; Brown, R. D.; Cherek, D. R.; Dailey, J. W.; Hilman, B.; Jobe, P. C.; Manno, B. R.; Manno, J. E.; Redetzki, H. M. Section on Clinical Pharmacology, Dept. of Pharmacology, Louisiana State University Medical Center, Shreveport, LA 71130 *Drug excretion in human breast milk: principles, pharmacokinetics and projected consequences*. *Clinical Pharmacokinetics*. 5(1):1-66, 1980.

The excretion of drugs in human breast milk was reviewed with regard to milk production, composition, feeding patterns, and mechanisms of drug transfer into milk. A pharmacokinetic approach useful in the study of most drugs was developed, and an infant modulated three compartment open model is proposed for drug distribution and elimination in breast feeding women. Milk/plasma drug concentration ratios are projected on the basis of pH partitioning. A neglected but potentially serious infant risk (impaired behavior and development) is discussed from the standpoint of emerging animal data. It is concluded that conceptually valid and comprehensive studies on drug excretion in breast milk are needed if this valuable nutrient is to be made available safely. 25 references. (Author abstract modified)

002496 Wilson, William H.; Petrie, William M.; Ban, Thomas A. Tennessee Neuropsychiatric Institute, 1501 Murfreesboro Road, Nashville, TN 37217 *Possible lack of anticholinergic effects with mianserin: a pilot study*. *Journal of Clinical Psychiatry*. 41(2):63-65, 1980.

Anticholinergic effects of mianserin, a new tetracyclic antidepressant, were studied in five depressed patients. Prior to and after 1 and 2 hours of the administration of 30mg of mianserin salivary flow, pupillary response to light and palpebral fissure were measured. Analysis of the data revealed a statistically significant increase in salivary flow and a statistically significant decrease in pupil diameter. There was no change in palpebral fissure size. These findings are consistent with other reports on mianserin reflecting not only a lack of anticholinergic activity, but also in the case of salivary flow, a possible increase in cholinergic activity. 6 references. (Author abstract modified)

002497 Winokur, Andrew; Rickels, Karl; Greenblatt, David J.; Snyder, Peter J.; Schatz, Norman J. Dept. of Psychiatry, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104 *Withdrawal reaction from long-term, low-dosage administration of diazepam: a double-blind, placebo-controlled case study*. *Archives of General Psychiatry*. 37(1):101-105, 1980.

In a double-blind placebo controlled case study, withdrawal symptoms are reported in a 32-year-old male who had been taking diazepam in doses of 15 to 25 mg/day during a 6 year period. Plasma levels of diazepam and its major metabolite, desmethyldiazepam, were monitored over the course of the study. Severe symptoms of physiological withdrawal were observed within 2 days of replacement of diazepam with placebo capsules. The patient recovered promptly on reinstitution of diazepam administration, and relapsed during a second withdrawal phase. During an additional 2 week period of placebo administration, the patient's condition first worsened, then gradually improved. Examination of plasma levels of diazepam and its major metabolite indicated no obvious pharmacokinetic abnormalities. Thus, with long-term administration of diazepam, withdrawal reactions may be encountered on abrupt termination. 27 references. (Author abstract modified)

002498 Wittenborn, J. R. Rutgers Interdisciplinary Research Center, Rutgers University, New Brunswick, NJ 08803 *Behavioral toxicity of psychotropic drugs*. *Journal of Nervous and Mental Disease*. 168(3):171-176, 1980.

A review of psychomotor response to psychotropic substances, restricted to normal subjects, is presented which describes responses to the initial standard dose of psychotropic substances in common use. Only placebo controlled studies which permitted statistical analysis of treatment group differences were considered for the summary. It is revealed that virtually all psychotropic substances have immediate detracting effects. The nature of the effects varies somewhat according to

the class of drug. It is suggested that this kind of information has safety implications which could influence the choice of medication. 10 references. (Author abstract)

002499 Worsley, Anthony. Division of Human Nutrition, C.S.I.R.O., Kintore Avenue, Adelaide, South Australia 5000, Australia **A prospective study of the effects of the progestagen content of oral contraceptives on measures of affect, automatization, and perceptual restructuring ability.** *Psychopharmacology*. 67(3):289-296, 1980.

Thirty-five young women completed the Profile of Mood States and tests of automatization and perceptual restructuring ability before and after commencing one of three forms of oral contraception or one form on intrauterine contraception (the loop). For each S on each experimental variable, the difference between the first and second tests was computed. These data were analyzed by covariance and discriminant function analyses. Two sets of functions were derived. The first distinguished the loop users from the oral contraceptive users. The latter exhibited significantly greater increases in anger and significantly greater reductions in vigor than the former. The second set of discriminant functions distinguished users of Neogynon from the women in the other three groups. Neogynon users' performances on the Color Words Test (a measure of automatization ability) worsened to a greater extent than was the case for members of the other groups. It is suggested that the changes in affect demonstrated by the first discriminant function were related to personal and attitudinal variables associated with the loop users. The second discriminant function was interpreted as an indication that the varying progestagen content of oral contraceptives may have differential effects upon both affect and automatization ability. 27 references. (Author abstract)

002500 Zeitner, Richard M.; Frank, Mary V.; Freeman, S. M. Dyrce. Prime Health Community Group Health Plan, 41st St. and Blue Ridge Cutoff, Kansas City, MO 64114 **Pharmacogenic and psychogenic aspects of galactorrhea: case report.** *American Journal of Psychiatry*. 137(1):111-112, 1980.

A case study is reported of galactorrhea occurring in a 40-year-old menopausal woman who had received neuroleptics for psychotic illness and who had elevated serum prolactin. This case highlights a composite interactional view of psychogenetic, endocrinologic and pharmacologic factors. Although the patient had been on neuroleptics for some time the symptom did not appear until she experienced the powerful wish to care for her daughter's baby. Her neuroleptic dosage was constant during the period when her galactorrhea peaked and then subsided, so the psychogenic aspects seemed to have controlled the timing of the galactorrhea. Although the galactorrhea decreased during psychotherapy it resolved only after trifluoperazine was discontinued. 9 references.

16 METHODS DEVELOPMENT

002501 Campbell, Iain C.; Shilling, David J.; Lipper, Steven; Slater, Stanley; Murphy, Dennis L. Clinical Neuropharmacology Branch, NIMH, Bethesda, MD 20205 **A biochemical measure of monoamine oxidase type A and B inhibitor effects in man.** *Journal of Psychiatric Research*. 15(2):77-84, 1979.

A method is described for the measurement of the effects of monoamine oxidase inhibitors (MAOI's) in human plasma. The procedure was used to estimate the levels of pargyline and clorgyline in plasma from patients with affective disorders. The results indicate that after an oral dose, pargyline is rapidly absorbed into the blood, reaches a maximum level in approximately 1 hour and has a half life of approximately 2 hours. After chronic administration, neither pargyline nor clorgyline attain steady state levels of MAOI inhibiting potential which are higher

than those seen 12 hours after a single dose of drug. A single 50mg dose of pargyline causes greater than 90% inhibition of platelet MAO; this dose of pargyline does not significantly alter plasma amine oxidase. It is suggested that the technique described is more suited to the measurement of the effects of pargyline than clorgyline. 16 references. (Author abstract modified)

002502 Cohen, Bruce M.; Lipinski, Joseph F.; Harris, Peter Q.; Pope, Harrison G., Jr.; Friedman, Matthew. McLean Hospital, 115 Mill St., Belmont, MA 02178 **Clinical use of the radioreceptor assay for neuroleptics.** *Psychiatry Research*. 2(2):173-178, 1980.

The potential clinical utility of the radioreceptor assay for neuroleptics (NRRA) was examined. The NRRA was able to detect neuroleptic activity in blood specimens from patients receiving a variety of neuroleptic medications. For each medication, mean plasma neuroleptic activity was lower in patients showing a poor response to treatment than in those showing a good response. Because the range of plasma neuroleptic activities found was quite different from drug to drug, it is suggested that results obtained by the NRRA must be standardized for each drug. 12 references. (Author abstract)

002503 Collins, Barry E.; Henker, Barbara; Whalen, Carol. Dept of Psychology, UCLA, Los Angeles, CA 90024 **A mixed crossover and parallel group design in psychopharmacological research -- example B.** *Psychopharmacology Bulletin*. 15(3):40-42, 1979.

The use of a mixed crossover and parallel group design to evaluate the effects of methylphenidate in hyperactive children is described. Data from the space flight dyadic communication task revealed an increase in communicative efficiency over trials only in the hyperactive children; this improvement may have been interpreted as a practice effect if the normal control group had not been included. Similarly, an increase in negative affect toward self in the medicated boys may have been mistakenly interpreted a positive response to the interruption of treatment without the data from the comparison group. Results indicate that elaboration of the classic two group crossover design to include an unmedicated comparison group adds important information available in the classic design. 5 references.

002504 Dudley, Donald L.; Volberding, Noel; Loebel, J. Pierre. Behavioral Medicine, Harborview Medical Center, 325 Ninth Avenue, Seattle, WA 98104 **Intravenous chlorimipramine and refractory depression.** *General Hospital Psychiatry*. 2(1):61-64, 1980.

A study in which 12 patients with refractory depression were treated with intravenous chlorimipramine to determine the safety and efficacy of this route of administration is reported. It was found that the intravenous route of administration is safe and without undue adverse reaction. Patients followed a similar course to those who experience oral treatment. It appears that there is a small number of patients in whom intravenous administration of antidepressants provides the route of choice. 9 references.

002505 Forrest, Irene S. University of San Francisco, San Francisco, CA 94117 **Chlorpromazine excretion: isotope vs chemical assay.** (Unpublished paper). Final Report, NIMH Grant R01-MH-25645, 1979. 10 p.

A methodology for monitoring blood/drug concentrations of the various clinically useful phenothiazines and their metabolites was developed and tested in man and rhesus monkey. Inclusion of the metabolites was considered essential to recognize differences in metabolic pathways (profiles). Specifically, preparative TLC was used to partition chlorpromazine (CPZ) and deriva-

tives extracted from urine into subgroups of metabolites. The TLC and GC/MS/COM data were compared with radioquantitation (isotopic) results, and it was found that CPZ is excreted more rapidly and completely than previously assumed. Some methodological conflicts in reconciling the amount of unmetabolized CPZ seen by TLC and GC were encountered.

002506 Innis, Robert B.; Tune, Larry; Rock, Robert; Depaulo, Raymond; U'Prichard, David C.; Snyder, Solomon H. Snyder: Dept. of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Tricyclic antidepressant radioreceptor assay**. *European Journal of Pharmacology*. 58(4):473-477, 1979.

A radioreceptor assay for tricyclic antidepressants was developed, based on the ability of the drugs to compete with tritiated quinuclidinyl benzilate for binding to muscarinic cholinergic receptors in rat brain membranes. When plasma samples from depressed patients treated with nortriptyline were assayed by the radioreceptor and gas/liquid chromatographic methods, results were nearly identical with the two techniques. The radioreceptor assay is sensitive and could detect 2ng/ml nortriptyline in plasma. However, the new assay should be used cautiously, if at all, in patients treated with other drugs that have potent anticholinergic effects. 10 references. (Author abstract modified)

002507 Jacobs, Keith W.; Nordan, Frances M. Dept. of Psychology, Loyola University, New Orleans, LA 70118 **Classification of placebo drugs: effect of color**. *Perceptual and Motor Skills*. 49(2):367-372, 1979.

To study the role of color in the psychological effects of placebo drugs, 100 subjects were asked to place each of six different colored capsules into one of three classifications of drug effects. Results indicate that red and yellow placebos are classified as stimulants while blue placebos are classified as depressants. Black placebos were given a depressant classification by students but not by nonstudents. It is assumed that the differential findings for students and nonstudents are the result of different prior experience with drugs of each color. It is concluded that segments of the population will differ in effects attributed on the basis of some colors and that blue seems universally to be seen as a depressant or tranquilizer. 7 references. (Author abstract modified)

002508 Kellner, Robert; Rifkin, Arthur; Rada, Richard T. Dept. of Psychiatry, University of New Mexico School of Medicine, Albuquerque, NM **The uses of the intensive design in psychopharmacology**. *Psychopharmacology Bulletin*. 15(3):35-37, 1979.

The use of the multiple cross-over design (intensive or subject-own-control design) in the evaluation of psychotropic drugs is discussed. The intensive design consists of measurements of responses to systematic repeated double-blind changes in treatment. This method permits separate assessment of drug effects in each patient, as well as differences in responses between patients. Idiosyncratic responses can be identified, and drug effects in subpopulations of the treatment group can be isolated. However, 12 or more treatment blocks are needed for an adequate analysis with this method, which makes it unsuitable for use in evaluating habituating drugs or drugs with a delayed onset of therapeutic action. 7 references.

002509 Kurata, Kouichi; Takeuchi, Masashi; Kido, Hideki; Yamaguchi, Nariyoshi. Dept. of Neuropsychiatry, Kanazawa University School of Medicine, Kanazawa, Japan **Quantitative flash-methylation analysis of phenobarbital**. *Folia Psychiatrica et Neurologica Japonica*. 33(3):311-314, 1979.

The quantitative flash methylation analysis of phenobarbital in biological fluids is described, and issues in the assay of anticonvulsant drugs by flash methylation are discussed. A common error on the assay of phenobarbital due to its decomposition by hydrolysis is noted, and the structure of the decomposition product of phenobarbital was determined by mass spectrometry (N-methyl-2-phenylbutyramide). 5 references.

002510 Narasimhachari, N.; Friedel, R. O.; Saady, J. J. Dept. of Psychiatry, Medical College of Virginia, Richmond, VA 23298 **Improved tricyclic antidepressant assay by GC/MS**. *Research Communications in Psychology, Psychiatry and Behavior*. 4(4):477-490, 1979.

A method for simultaneous determination of both tertiary and secondary amine tricyclic antidepressants in a single injection is reported. D4-imipramine and d4-desipramine are used as internal standards and bis N-methyl trifluoroacetamide is used as the derivatizing reagent. The ions monitored for the endogenous drugs and the internal standards differ by at least 4 units and therefore eliminate any interference by (m1) and (m2) ions. This method eliminates the need for two injections of the sample in the procedure described by Wilson et al., 1977. The use of d4-internal standards for all of the drugs removed a possible source of error in the use of one drug as an internal standard for the quantitation of another drug in plasma, since patients might be on more than one tricyclic antidepressant. 14 references. (Author abstract modified)

002511 Othmer, Ekkehard; Powell, Barbara; Piziak, Veronica K.; Preskorn, Sheldon H. Preskorn: Dept. of Psychiatry and Pharmacology, University of Kansas School of Medicine, 39th & Rainbow Blvd., Kansas City, KS 66103 **Prospective use of saliva lithium determinations to monitor lithium therapy**. *Journal of Clinical Psychiatry*. 40(12):525-526, 1979.

The utility of a mathematical equation ($y = 2.27x - 0.45$) relating saliva (y) to plasma (x) lithium concentrations was evaluated in a prospective study of 25 new manic patients. The correlation coefficient between the predicted and the observed plasma concentration was $r = 0.89$. Results demonstrate that saliva lithium determinations may be safely used to monitor lithium therapy. 9 references. (Author abstract modified)

002512 Pluym, Achille. Analytical Dept., Janssen Pharmaceutica, B-2340 Beerse, Belgium **TLC differentiation of butyrophenone and diphenylbutylpiperidine compounds from phenothiazine derivatives**. *Journal of Pharmaceutical Sciences*. 68(8):1050-1052, 1979.

A procedure is described for thin layer chromatographic (TLC) detection and differentiation of the butyrophenone/diphenylbutylpiperidine group and phenothiazine derivatives at the microgram level. A two dimensional TLC method to separate butyrophenone and diphenylbutylpiperidine compounds is reported. A variety of possible detection reagents was examined. The solvent systems and spray reagents described should be useful for the identification of these drugs in various dosage forms. 18 references. (Author abstract)

002513 Ross, Donald C.; Klein, Donald F. New York State Psychiatric Institute, 722 W 168th St., New York, NY 10032 **A comparison of analysis of covariance and the theta tilde technique as applied to illustrative psychopharmacological data**. *Journal of Psychiatric Research*. 15(2):67-75, 1979.

A method of data analysis, the theta tilde technique, aimed at detecting differences in response patterns to drug and placebo is described. Instead of positing a linear relationship between pre-treatment and posttreatment scores and then testing for differences between slopes or between adjusted posttreatment means,

the pretreatment by posttreatment data matrix is partitioned into drug typical and placebo typical regions. One may stipulate beforehand the shape of these regions and a significance test of whether the partition discriminates between the groups is provided. Alternately, one may search a number of partitions, and a significance test over the set of searched partitions is provided. The method is illustrated with real psychopharmacological data and the results are compared with ANO-COVA. It appears that the null hypothesis of no differences between treatments is rejected in approximately the same set of items with some indication of superior power for the theta tilde technique. 6 references. (Author abstract modified)

002514 Sjoqvist, F. Dept. of Clinical Pharmacology, Karolinska Institute, S-141 86 Huddinge, Sweden **Monitoring of antidepressant drug plasma levels: the next ten years.** Progress in Neuro-Psychopharmacology. 3(1-3):201-210, 1979.

The monitoring of antidepressant drug plasma levels as indicators of therapeutic efficacy and individual drug metabolism is described, and suggestions for future research on the relationship between plasma level and drug response are offered. It is noted that each of the antidepressant drugs has individual pharmacokinetic and pharmacodynamic properties, and it is unlikely that one drug will be effective in all patients. Novel rapidly acting drugs are desirable because the slow onset of action of tricyclic antidepressant seriously hampers their clinical evaluation. Methodological improvements in the drug analytical methods and in the criteria for selecting and rating study patients with depressive disorders are urged. 51 references. (Author abstract modified)

002515 Smith, Robert V.; Humphrey, David W.; Wilcox, Richard E. Drug Dynamics Institute, College of Pharmacy, University of Texas, Austin, TX 78712 **Stability of apomorphine in frozen plasma samples.** Research Communications in Chemical Pathology and Pharmacology. 27(1):183-186, 1980.

Three rather simple procedures for storage of apomorphine containing plasma samples are examined. Apomorphine was relatively stable in frozen plasma samples for 4 weeks. Addition of 5mM ascorbic acid extended stability to at least 10 weeks. Dithiothreitol and bisulfite were less effective and may have formed complexes that prevented complete extraction of apomorphine from plasma. 12 references. (Author abstract modified)

002516 Stewart, J. T.; Honigberg, I. L.; Tsai, A. Y.; Hajdu, P. Honigberg: Bioavailability Group Studies, School of Pharmacy, University of Georgia, Athens, GA 30602 **Fluorometric determination of clobazam, a 1,5-benzodiazepine, in human plasma.** Journal of Pharmaceutical Sciences. 68(4):494-496, 1979.

A fluorometric procedure for clobazam, a 1,5-benzodiazepine, is described, which is based on a fluorophore formed upon irradiation of the drug using short wavelength UV light (254nm) for 35 minutes. Fluorescence is linear over a 100 to 6400ng/ml range using excitation and emission wavelengths of 350nm and 400nm, respectively. Application of this method to the determination of clobazam in spiked human plasma samples showed the drug could be determined at nanogram per milliliter levels with an accuracy of 1 to 5%. The procedure is specific for clobazam in samples containing its major plasma metabolite, N-desmethyl-clobazam, and in samples containing 1,4-benzodiazepines and other selected drugs. A plasma level/time profile after oral administration of a single 40mg dose of clobazam to a healthy adult male is presented. 9 references. (Author abstract modified)

002517 Stewart, M. J.; Ballinger, B. R.; Macaulay, K. E. C.; Devlin, E. J.; Ramsay, A. C. Department of Clinical Chemistry, Edinburgh Royal Infirmary, Edinburgh, Scotland **Adjustment of plasma phenytoin levels using a nomogram in mentally handi-**

capped and psychiatric patients. British Journal of Mental Subnormality. 25(48):27-30, 1979.

The nomogram of Richens and Dunlop (1975) was used to predict phenytoin dosage for patients in a mental subnormality and a psychiatric hospital. In those cases where clinicians implemented the suggested dose change, 75% of patients achieved plasma levels within the therapeutic range. The results were compared with the situation before nomogram predictions were available, when 52% of dose changes resulted in levels within the desired range. 5 references. (Author abstract)

002518 Sun, Sy-Rong; Hoffman, D. J. Pharmaceutical Produce Division, Abbott Laboratories, North Chicago, IL 60064 **Rapid, sensitive GLC determination of pentobarbital and other barbiturates in serum using nitrogen-specific detector.** Journal of Pharmaceutical Sciences. 68(3):386-388, 1979.

A gas/liquid chromatographic method for the analysis of pentobarbital in serum was developed. After extraction from serum, a methyl derivative was prepared and quantitated by nitrogen specific detection. Secobarbital was used as the internal standard. The method has a sensitivity of 0.08mcg/ml for pentobarbital with only 0.1ml of serum. 14 references. (Author abstract modified)

002519 Sutfin, Tamara A.; Jusko, William J. Jusko: Clinical Pharmacokinetics Laboratory, Dept. of Pharmaceutics, School of Pharmacy, SUNY, Buffalo, NY 14209 **High-performance liquid chromatographic assay for imipramine, desipramine, and their 2-hydroxylated metabolites.** Journal of Pharmaceutical Sciences. 68(6):703-705, 1979.

A high performance liquid chromatographic (HPLC) method for the simultaneous determination of imipramine, desipramine, and their 2-hydroxylated metabolites in plasma is described. The method involves a simple plasma extraction at basic pH with organic solvent, chromatography on a silica gel column, and fluorescence detection. High fluorescence sensitivity permits detection of 1ng of each drug and metabolite in 1ml of plasma. Results obtained with the HPLC method showed excellent correlation with those obtained via a gas-liquid chromatographic/mass spectrometric method for desipramine, but the HPLC assay yielded higher results for imipramine. 18 references. (Author abstract modified)

002520 Sweet, James S. Room 200, 5801 S. Ellis Avenue, Chicago, IL 60637 **New blood test measures chemical associated with manic-depressive states.** University of Chicago Reports. 27(2):6-7, 1979.

The development of a gas liquid chromatography/electron capture blood test that reflects varying levels of 3-methoxy-4-hydroxyphenylglycol (MHPG) in manic and depressive states is described. Tests of over 60 manic and depressed patients have demonstrated that the test reliably reflects noradrenergic activity in the brains of such patients before and during medication, and it correlates well with their mood and response to treatment. High level of MHPG during mania decline dramatically after treatment with lithium carbonate, and low levels of MHPG during depression increase following tricyclic antidepressant drug administration.

002521 Tune, Larry; Coyle, Joseph T. Dept. of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, 725 N. Wolfe St., Baltimore, MD 21205 **Serum levels of anticholinergic drugs in treatment of acute extrapyramidal side effects.** Archives of General Psychiatry. 37(3):293-297, 1980.

A simple, sensitive, and specific radioreceptor assay was developed for measuring anticholinergic drugs in human serum.

The assay is based on the competitive inhibition by free anticholinergic drugs in a 0.2-ml sample of serum with the specific binding of the potent muscarinic antagonists, tritiated quinuclidinyl benzilate, to solubilized brain muscarinic receptors. Anticholinergic activity could be detected regardless of drug structure and was qualified against atropine standards. Although the serum levels of anticholinergic drugs varied considerably in 35 patients receiving both neuroleptic and anticholinergic drugs, there was a highly significant inverse correlation between the presence of acute extrapyramidal side-effects due to neuroleptics and the serum levels of anticholinergics. 23 references. (Author abstract)

002522 Uhlenhuth, E. H.; Glass, Richard M.; Fischman, Marian W. Dept. of Psychiatry, University of Chicago, Chicago, IL Multiple crossover designs with an antianxiety agent and an antidepressant. *Psychopharmacology Bulletin*. 15(3):37-40, 1979.

The use of a multiple cross-over, small sample design to detect the effects of psychotropic drugs is described. Significant therapeutic effects of diazepam and imipramine were detected with the multiple cross-over design but were not apparent when conventional procedures were used. Factors that may contribute to the lower sensitivity of the subject-own-control approach are discussed. 9 references.

002523 Whitaker, Patricia Mack. University of Toronto (Canada) Brain receptors for LSD and serotonin. (Ph.D. dissertation). *Dissertation Abstracts International*. 40(8):3674-B, 1980. (Not available from Univ. Microfilms), 1979.

Two new direct binding assays were developed for central serotonin receptors using the two radioligands commonly used to label serotonin receptors, serotonin itself and d-LSD. Competition curves were determined for a variety of drugs with the following results: serotonin was the only neurotransmitter which had activity, the drugs related to tryptamine or ergot had significant activity, and no anticonvulsants, antidepressants, antihistamines, sedative/hypnotics showed any activity. The difference in binding distribution of the two radioligands and the differing potencies of the tryptamines at competing for the bound radioligands led to the suggestion that the two ligands were not labeling identical sites. (Journal abstract modified)

17 MISCELLANEOUS

002524 Adler, Martin W. Dept. of Pharmacology, Temple University School of Medicine, Philadelphia, PA 19140 **Opioid peptides**. Life Sciences. 26(7):497-510, 1980.

Current status and research trends in the field of endogenous opiate-like substances (opioid peptides) are reviewed. The enormous volume of research publications on the endogenous opioids during the decade of the 1970s is noted, and a brief historical review of the field is presented. Issues related to terminology, receptor types, tolerance and dependence, and anatomical loci are discussed. Practical difficulties in research on the physiological functions and pharmacological actions of these compounds are described. 74 references.

002525 Allen, Robert E.; Pitts, Ferris N., Jr.; Summers, William K. 1934 Hospital Place, Los Angeles, CA 90033 **Drug modification of ECT: methohexital and diazepam. II**. Biological Psychiatry. 15(2):257-264, 1980.

A systematic comparison of methohexital and diazepam as anesthetics in the drug modification of electroconvulsive therapy (ECT) was done by holding atropinization, succinylcholine depolarizing neuromuscular blockade, and resuscitation constant while monitoring four ECTs in each of 24 patients. The data revealed significant differences and methohexital was superior. Significantly more ventricular premature contractions occurred after diazepam. Diazepam records contained both more numerous and more extensive EKG abnormalities. It is concluded that methohexital has been demonstrated to be the anaesthesia of safety and choice for ECT when compared to diazepam. 12 references. (Author abstract modified)

002526 AmaraSingham, Lorna Rhodes. 6012 Welborn Drive, Bethesda, MD 20016 **Social and cultural perspectives on medication refusal**. American Journal of Psychiatry. 137(3):353-358, 1980.

The sociocultural anthropology of medication refusal is examined in relation to the concept of compliance, and the social and cultural meaning of medication both within and outside the treatment setting. In addition to physician-patient communication and the patient's understanding of the illness and the regimen, drug compliance is affected by social and cultural factors which influence the patient's attitudes toward and meanings of illness and its treatment. For instance, the hot/cold explanatory model used by the Puerto Rican or the humoral model of the Chinese affect these patients' conception of illness and treatment expectations. Even when physician and patient are from the same cultural background basic discrepancies between the biomedical and ethnomedical categories used by each may result in noncompliance. In addition to the beliefs and attitudes patients bring to treatment with them, the treatment setting itself has an impact: the hospital, the physician's office, and the community mental health center may convey quite different messages about medication, and the patient's willingness to comply with a regimen may reflect the social environment in which it is proposed. Thus, medication refusal may represent the patient's attempt to reject detrimental labels or to act in accordance with his own conceptual model of what is wrong with him. 28 references. (Author abstract modified)

002527 Ananth, J. 687 Pine Avenue West, Montreal, Quebec H3A 1A1, Canada **Predicting response to antidepressants**. Psychosomatics. 21(1):25, 29-31, 1980.

The variables that affect a patient's therapeutic response to antidepressants are reviewed, appropriate medications are dis-

cussed, and future research directions are explored. Demographic and personal variables that affect the response to antidepressants include premorbid personality, age, sex, genetic and family history, and ethnicity. The diagnosis of premorbid personality, including cyclothymic, neurotic, or normal, has value in predicting drug response. In view of the possible genetic link influencing patient's response to antidepressants, a careful family history should be useful in every known case of depressive episode. Family history of illness itself may be useful in predicting drug response. 41 references.

002528 Angle, Hugh V. Dept. of Psychiatry, Duke University Medical Center, Box 3870, Durham, NC 27710 **Sleep problems and sleep medication involvement of psychiatric patients**. Journal of Nervous and Mental Disease. 167(12):752-757, 1979.

The sleep problems and sleep medication involvement of psychiatric patients were investigated via a computer interview that assessed 27 life problem areas. Within the sleep area, difficulty falling asleep was compared to awakening problems and appears to be a more severe patient problem in terms of the large number of associated nonsleep problems. Patients' intensity of physical tension and degree of excessive solitary behavior was found to be related to the problem of falling asleep. The major variables associated with awakening problems were pain and physical complications interfering with sleep. Patients with a strong medication involvement were found to use multiple classes of drugs, to use a greater overall quantity of drugs, and to express various drug problems. A combination of physical tension, anxiety, and depression were predictive of patients' sleep medication involvement, whereas no one particular group of sleep problems indicated a significantly greater involvement than another group. 18 references. (Author abstract modified)

002529 Appelbaum, Paul S.; Gutheil, Thomas G. Gutheil: 74 Fenwood Road, Boston, MA 02115 **Drug refusal: a study of psychiatric inpatients**. American Journal of Psychiatry. 137(3):340-346, 1980.

Psychiatric inpatient refusal of medication was examined over a 3 month period in a 40 bed inpatient unit of a community mental health service. Over this period, there were 23 medication refusers (overt, explicit refusal) accounting for 72 individual episodes of refusal. Analysis of data revealed three distinct groups of refusers: 1) situational refusers who on occasion refused medication for a brief period of time and for one of a variety of reasons; 2) stereotypic refusers consisting of chronically ill patients with paranoid traits who habitually and predictably responded to a variety of stresses with brief medication refusal; and 3) symptomatic refusers who were young, relatively acutely ill patients, whose refusal, often based on delusional premises, was sustained over a long period and successfully stymied treatment efforts. Only for the five patients in this last category (symptomatic refusers) was care seriously impaired. Psychological and clinicoforensic issues in medication refusal are discussed; and it is suggested that legal conceptions of a right to refuse treatment may not accurately reflect clinical realities, in which the patients' refusal is determined by the dynamics of their illness rather than reflecting a principled exercise of their legal rights. 28 references. (Author abstract modified)

002530 Baldessarini, Ross J. Mailman Research Center, McLean Hospital, 115 Mill Street, Belmont, MA 02178 **Status of psychotropic drug blood level assays and other biochemical measurements in clinical practice**. American Journal of Psychiatry. 136(9):1177-1180, 1979.

The present clinical value of laboratory biochemical measurements in psychiatry is discussed. Assays of drug levels in blood and of other biochemical characteristics of psychiatric patients are proposed for clinical application, although their utility in practice remains uncertain. Exceptions are the assays of blood levels of anticonvulsants and of lithium ion. Assays of antidepressant drugs may be especially helpful in the evaluation of unexpected responses or in the avoidance of unwanted toxic effects, and promise to permit more efficient predictions of individual requirements. Assays of platelet MAO activity or urinary MHPG excretion remain clinically less useful. Attempts to correlate blood levels of antipsychotic agents with clinical effects have been disappointing, although newer assay methods may prove more useful. However, it is cautioned that the uncritical, uninformed, and prematurely promiscuous application of these technologies requires restraint lest they become a needless expense and a way of avoiding the traditional interpretation of clinical signs and changes in the status of individual patients. 14 references. (Author abstract modified)

002531 Barnes, Robert; Raskind, Murray. Veterans Administration Hospital, 4435 Beacon Avenue, South, Seattle, WA 98108 **Strategies for diagnosing and treating agitation in the aging.** *Geriatrics*. 35(3):111-115, 119, 1980.

Agitation, a behavioral term connoting excessive motor activity, is discussed in terms of its symptoms and treatment. Agitation can present with behavioral symptoms that may arise from multiple causes. Because of this, it is important not to respond automatically by prescribing psychotropic medication. Effective treatment is important because it may allow the elderly patient to receive proper medical attention, continue to live home, or lead a more humane existence in a nursing home. The side-effects of antipsychotic medication must be well understood by physicians. Familiarity with antipsychotic drugs of both low anticholinergic activity, such as haloperidol and thiorixene, as well as those with low extrapyramidal activity, such as thioridazine, is required. 8 references.

002532 Beattie, B. L.; Sellers, E. M. Sellers: 33 Russell St., Toronto, Ontario M5S 2S1, Canada **Psychoactive drug use in the elderly: the pharmacokinetics.** *Psychosomatics*. 20(7):474-479, 1979.

General pharmacokinetic principles applicable to geriatric patients are reviewed and practical guidelines for the use of psychoactive drugs based on these principles provided. Elderly patients are given medications more frequently and adverse reactions are more common. Incomplete understanding, dosage errors, self-medication, and poor compliance are common in patients living alone or with impaired mental capacity. Chronic disease processes and possibly aging itself alter responsiveness to drugs. Knowledge and application of pharmacokinetic principles can prevent inappropriate and unnecessary use of drugs and promote thoughtful prescriptions. It is concluded that pharmacotherapy in older patients is safe as long as patients are monitored frequently and any necessary adjustments in drug dosages are made. 24 references.

002533 Beckmann, B.; Hippus, H.; Ruther, E. Hippus: Psychiatrischen Klinik der Universität München, Nussbaumstrasse 7, D-8000 Munich 2, Germany **Treatment of schizophrenia.** *Progress in Neuro-Psychopharmacology*. 3(1-3):47-52, 1979.

The twenty-five year history of the chemotherapy of schizophrenia with neuroleptics is briefly reviewed. The development of certain butyrophenones more directly effective in minus symptoms of schizophrenia and the introduction of depot neuroleptics are discussed. Extrapyramidal motor side-effects of neuroleptics are described, and the therapeutic promise of clozapine is noted. The use of the neuroleptics as tools for the exploration

of the etiopathogenesis of schizophrenia is discussed. 32 references. (Author abstract modified)

002534 Berger, Philip A.; Rexroth, Katharine. VA Hospital, Ward 4C2, 3801 Miranda Avenue, Palo Alto, CA 94304 **Tardive dyskinesia: clinical, biological, and pharmacological perspectives.** *Schizophrenia Bulletin*. 6(1):102-116, 1980.

A clinical, biological, and pharmacological overview of tardive dyskinesia is presented. Prevalence reports of tardive dyskinesia range from 0.5 to 56%, with a mean reported prevalence of 15% in institutionalized patients. A variety of pharmacological agents have been investigated as possible treatments for tardive dyskinesia, including agents that decrease central dopaminergic activity, cholinomimetics, and agonists of gamma-aminobutyric acid. Cholinomimetics currently show the greatest potential for improving the symptoms of tardive dyskinesia. New and effective treatments for tardive dyskinesia need to be developed and clinically tested; new antipsychotic agents that do not produce tardive dyskinesia are also needed. 123 references. (Author abstract modified)

002535 Bergman, U.; Christenson, I.; Jansson, B.; Wiholm, Bengt-Erik. Wiholm: Dept. of Clinical Pharmacology, Huddinge University Hospital, S-141 86 Huddinge, Sweden **Auditing hospital drug utilisation by means of defined daily doses per bed-day: a methodological study.** *European Journal of Clinical Pharmacology*. 17(3):183-187, 1980.

The utilization of hypnotics, sedatives, and minor tranquilizers (HSmT) was audited in a Swedish university hospital for 1975 to 1977 by means of drug delivery and hospital occupancy statistics. A total of 0.53 defined daily doses (DDD) per bed day were delivered in 1975, implying that every second patient might have regularly been prescribed HSmT. The benzodiazepines were predominant with 71% of the deliveries. Five major drugs accounted for 88% of DDD. The drug pattern and the range of DDD per bed day differed considerably between the hospital departments. Drugs not recommended by the hospital's Pharmacy and Therapeutics Committee accounted only for 3% of deliveries. In a drug surveillance study performed in two medical wards, HSmT were prescribed for 43% of 274 patients. Drug delivery and prescription data were in broad agreement. Drug information activities in the hospital had a clearly discernable influence on the delivered DDD per bed day. This measure is judged an inexpensive indicator of drug utilization in a hospital and a suitable basis for therapeutic audit. 16 references. (Author abstract)

002536 Bielski, Robert J.; Friedel, Robert O. Department of Psychiatry, Michigan State University, East Lansing, MI 48823 **Depressive subtypes defined by response to pharmacotherapy.** *Psychiatric Clinics of North America*. 2(3):483-497, 1979.

Four different depressive subtypes which appear differentially responsive to four different classes of psychiatric medications or combinations thereof are described. The diagnostic categories of unipolar, bipolar, atypical, and psychotic depressions are discussed under the headings of tricyclic antidepressants, lithium, monoamine oxidase inhibitors, and antipsychotic agents, respectively. Acute and prophylactic effects of medication are addressed and case studies are given. It is concluded that significant progress in psychopharmacological and biological research offers promise for the rational treatment of the various biochemical or neurophysiological subtypes of depression. 112 references.

002537 Bossier, J.-R. no address **Differential psychopharmacology of anxiolytics and sedatives.** Basel, S. Karger. 1979. 173 p. \$32.50.

The subdiscipline of psychopharmacology concerned with the description, explanation, and prediction of individual differences in response to psychotropic drugs is discussed. Psychological literature on tranquilizing and sedating drugs are reviewed. Clinical, behavioral, and neuropharmacological studies of tranquilizing and sedating compounds are presented.

002538 Brewer, Colin no address **Pain at the Mayo.** World Medicine. 15(2):34-35, 1979.

New approaches to the relief of pain being investigated at the Mayo Clinic are described. Dr. Joseph Wang has pioneered the use of intrathecal narcotics. It has been shown that very small doses of narcotic drugs—as low as 1mg of morphine—can produce profound pain relief when injected into the CSF, generally without the usual systemic effects. This is presumably due to the high concentration of endorphin receptors in the spinal cord. Unlike spinal anesthesia, intrathecal morphine relieves pain without interfering with other forms of sensation. A single injection can provide pain relief for up to 24 hours, and Wang hopes that it will soon be possible to provide continuous infusion for longer periods through a spinal catheter. For patients with intractable pain, the psychiatric department of St. Mary's Hospital has a pain management clinic where patients are taught to live with pain which cannot be relieved by physical means. It uses a behavioral approach and works on the principle that for some patients pain and certain responses to pain have become habits which may be neither appropriate nor useful, and that these habits can sometimes be changed. Excluding family visits until the end of the treatment period gives the psychiatrists and nursing staff a better chance of altering the patient's pattern of behavior. The principles of behavior are apparently simple and relevant to everyday life.

002539 Cavenar, Jesse O., Jr.; Harris, Michael A. Psychiatry Service, Veterans Administration Medical Center, 508 Fulton St., Durham, NC 27705 **A American Journal of Psychiatry.** 137(1):99-100, 1980.

The case history of a husband and wife who shared similar dystonic symptoms and psychotic level identification and fusion that led to diagnostic difficulty is reported. Both reported to the emergency room of a hospital with clenched teeth and bizarre posturing. The man's dystonic reaction was caused by an accidental dose of haloperidol. His symptoms were immediately eliminated by diphenhydramine. The wife's symptoms were caused by a psychotic level identification and fusion with her husband. When she was reassured of her husband's recovery she recovered spontaneously. 4 references.

002540 Chilton, W. Scott; Bigwood, Jeremy; Jensen, Robert E. Dept. of Chemistry, University of Washington, Seattle, WA 98195 **Psilocin, bufotenine and serotonin: historical and biosynthetic observations.** Journal of Psychedelic Drugs. 11(1-2):61-69, 1979.

The historical use, manufacture, and biosynthetic composition of psilocin, bufotenine, and serotonin are described. Research has shown that they all are natural central nervous system neurotransmitters. Psilocin, serotonin and bufotenine have all been found in toadstools and in some cases psilocin and bufotenine occur together in the same mushroom. The biogenetic relationships between psilocin, serotonin, and bufotenine are illustrated. 15 references.

002541 Clark, Robert B. Hoffman-LaRoche, Inc., Nutley, NJ **Is the abuse of valium exaggerated?** Resident & Staff Physician. 25(11):94, 1979.

Patterns of prescription and the use of psychoactive drugs were examined in an NIMH supported study of 2,552 individ-

uals. Results indicate that 15% of subjects had had a minor tranquilizer prescribed for them during the preceding year and that psychotherapeutic drug use was clearly and strongly related to levels of psychic distress and life crisis. In a similar study undertaken with samples from nine Western European countries, the United States was ranked sixth or seventh among 10 nations in levels of psychoactive drug use. These results refute the widely held belief that such drugs are commonly prescribed for minor and transient disturbances and suggest that the extent of use of psychoactive drugs in the US is neither unique nor atypical.

002542 Coble, Patricia A.; Kupfer, David J.; Spiker, Duane G.; Neil, John F.; McPartland, Richard J. Kupfer: Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15261 **EEG sleep in primary depression: a longitudinal placebo study.** Journal of Affective Disorders. 1(2):131-138, 1979.

The persistence and/or variability of the findings that characteristic EEG sleep changes in depression are highlighted by sleep continuity disturbance, delta sleep reduction, and shortened REM latency were examined. The sleep of 12 hospitalized, nondelusional, primary depressives who were involved in a program of active psychosocial treatment intervention and received only placebo during a 5 week study period was examined nightly. Findings show a lack of change across time, particularly in parameters associated with a primary or biologic depressive episode. While some degree of clinical improvement was noted, the group failed to achieve a state of remission or even partial remission as determined by the Hamilton Rating Scale. It appears that the major sleep alterations associated with such disorders persist for up to at least 5 weeks in the absence of pharmacologic or other somatic intervention. 27 references. (Author abstract modified)

002543 Concept Media (C-M), distributor. C-M: PO Box 19542, Irvine, CA 92714 **Drugs: Autonomic and Somatic Nervous Systems.** 35mm filmstrips cassettes or records sound sale multimedia

Presents graphic and narrated information on the effects of drugs on the autonomic and somatic nervous systems. The seven programs are: anatomy and physiology, cholinergics, cholinergic blockers, adrenergics, sympathetic inhibitors (in two parts), and clinical applications. Emphasizes the interactions of drugs and warns about side-effects. Appropriate in training physicians, nurses, and others who manage patients receiving drugs as medication, as well as in drug abuse and alcohol education since prescription drugs are often used by substance abusers. Available with workbooks.

002544 Dalton, Katharina. no address **Intelligence and prenatal progesterone: a reappraisal.** Journal of the Royal Society of Medicine. 72(6):397-399, 1979.

The relation of progesterone administered during the first trimester of pregnancy to the subsequent intelligence of the children was retrospectively studied. Thirty-two children, aged 6 to 13 years, whose mothers had received progesterone were selected from the practice records, and their academic records were compared with those of 32 matched controls whose mothers had not received progesterone. Fifty-five percent of those children whose mothers had received progesterone were above average academically, while only 41% of controls were above average. A subsequent study confirmed the superiority of the progesterone children in academic subjects, but not in craftwork or physical education. Findings indicate that any benefit to the child from the effect of progesterone occurs only if that progesterone is administered before the 16th week of pregnancy. 12 references.

002545 Davis, John M.; Schaffer, Charles B.; Killian, Grant A.; Kinard, Carl; Chan, Carl. Illinois State Psychiatric Institute, 1601 W. Taylor Street, Chicago, IL 60612 **Important issues in the drug treatment of schizophrenia.** *Schizophrenia Bulletin*. 6(1):70-87, 1980.

The large body of research demonstrating the effectiveness of antipsychotic drugs in the treatment of acute schizophrenia is selectively reviewed. Research evidence relevant to the following issues is assessed: indications for selective treatment; characteristics of drug responders and nonresponders; indications for high dosage phenothiazine treatment; indications for maintenance therapy; and the benefits and risks of antipsychotic drugs. Recommendations are made concerning areas of psychopharmacologic research that require further development. 66 references. (Author abstract)

002546 Dennis, P. J. Bradford-on-Avon, Wiltshire, England **Monitoring of psychotropic drug prescribing in general practice.** *British Medical Journal*. No. 6198:1115-1116, 1979.

Patients who requested repeated prescriptions of psychotropic and hypnotic drugs without requesting a consultation with a doctor were audited. Over 1000 repeat prescriptions of psychotropic drugs were analyzed from a population of over 100,000 patients. The analysis showed that the longer repeat prescribing had taken place, the older the patient was likely to be and the less closely were they monitored by their general practitioner. It is concluded that long-term repeat prescribing represents a failure in doctor-patient communication. 11 references. (Author abstract modified)

002547 Diaz, Jose Luis. Instituto de Investigaciones Biomedicas, Universidad Nacional Autonoma de Mexico, Apartado Postal 70228, Mexico 20 D.F., Mexico **Ethnopharmacology and taxonomy of Mexican psychodysleptic plants.** *Journal of Psychodelic Drugs*. 11(1-2):71-101, 1979.

Mexican psychodysleptic plants are classified according to their ethnopharmacologic effects and taxonomic scheme. Botanical species are described both in terms of their traditional uses and their psychological and neurobiological effects. In the class of psychodysleptics six families are differentiated: hallucinogens, trance-inducers (ololiuqui, sinicuiche), cognodysleptics (marihuana, calezacatechichi), delirants (tropane and piperidine solanaceae), neurotoxins (papilionidae), and narcotics. All these drugs have the ability to induce special states of consciousness which are qualitatively different from the ordinary. The medical and analgesic uses of these plants are emphasized. 156 references.

002548 Dudley, Donald L.; Rowlett, David B.; Loebel, Pierre J. Harborview Medical Center, ZA-99, 325 Ninth Avenue, Seattle, WA 98104 **Emergency use of intravenous haloperidol.** *General Hospital Psychiatry*. 1(3):240-246, 1979.

The emergency use of intravenous haloperidol in 20 cases in which mental state was gravely impaired, prohibiting necessary investigation and treatment of physical disabilities is reviewed. This use of haloperidol was efficacious and uncomplicated, although not specifically FDA approved. Comparative studies of intravenous efficacy of neuroleptics are urged. 8 references. (Author abstract modified)

002549 Epstein, Richard S. 10401 Old Georgetown Rd., Bethesda, MD 20014 **Withdrawal symptoms from chronic use of low-dose barbiturates.** *American Journal of Psychiatry*. 137(1):107-108, 1980.

A case history of a woman who developed a mild but persistent hallucinosis and other symptoms suggestive of withdrawal after discontinuing abruptly the use of phenobarbital in low

doses is reported. To offset this syndrome the dosage of phenobarbital was reinitiated and tapered off gradually over a six week period. Clinicians are warned of the possibility that even low dose barbiturate use may result in withdrawal symptoms on abrupt cessation with certain patients. 9 references.

002550 Fahy, T. J.; Carney, P. A.; Shields, K. Dept. of Psychiatry, University College of Galway, Regional Hospital, Galway, Ireland **Sleeping pills for psychiatric patients.** *Lancet*. No. 8151:1072, 1979.

The creation of a sleeping pill free milieu in the psychiatric unit of a general hospital is described, and the hazards of over-prescription of sleeping pills to psychiatric patients are discussed. Newly admitted patients requesting hypnotics are told of the firm unit policy against night sedation and are not given any reason to expect that exceptions can be made in individual cases. Except for a handful of addicted patients being detoxified, no patient has yet found it necessary to depart against medical advice because of failure to obtain sleeping pills. The need for defining indications (if any) for sleep inducing drugs in the management of major psychiatric illness is emphasized.

002551 Flowers, Retha Vivian Wellons. University of Michigan **Effects of social support on adherence to therapeutic regimens.** (Ph.D. dissertation). Dissertation Abstracts International. 39(10):5113-B, 1979. Ann Arbor, Univ. Microfilms No. 7907073, 195p., 1978.

The conceptualization and manipulation of social support and the mechanism by which social support increases adherence to therapeutic regimens and consequent goal attainment were investigated. The effects of objective social support on adherence to antihypertensive regimens among 236 outpatient adults were studied. The results generally agree with previous evidence that showed social support to be positively associated with goal attainment. Findings from analyses by experimental groups imply that the pathway by which objective social support effects adherence and goal attainment is primarily through perceived social support and objective knowledge to the therapeutic regimen. For the social support with partner group, the increase in the proportion of people with a controlled blood pressure was significantly higher than for either the social support or control groups. Implications for future research are proposed in the area of theory testing. (Journal abstract modified)

002552 Ford, Maurice Deg. 74 Fenwood Road, Boston, MA 02115 **The psychiatrist's double bind: the right to refuse medication.** *American Journal of Psychiatry*. 137(3):332-339, 1980.

Issues surrounding the patient's right to refuse medication are discussed. Such a refusal places the psychiatrist in a double bind: a certain medication may greatly relieve mental disturbance, yet forcing the patient to receive medication undermines the patient's sense of autonomy. In the case of involuntarily committed patients, the psychiatrist may be legally liable for failing to provide treatment or for not respecting the patient's right to refuse treatment. The constitutional origins of the right to refuse treatment, the state's interest in mandating treatment, and legal and ethical considerations in the treatment of mental illness are examined. It is suggested that in many cases, delaying medication until a patient is formally judged incompetent causes discomfort for the patient, the physician, the staff, and other patients. In addition to the potentially negative effects of legal guardianship on the therapeutic alliance and on the patient's sense of personal responsibility and autonomy, the failure to medicate during the pendency of guardianship procedures raises some fundamental questions involving a number of conflicting rights. The right to refuse medication presents a uniquely intriguing case study of a need for accommodation between ab-

abstract constitutional concepts and practical realities and has opened a profound legal and ethical debate about the nature of true freedom. 29 references. (Author abstract modified)

002553 Forster, E. F. B. Dept. of Psychiatry, University of Ghana Medical School, P. O. Box 4236, Accra, Ghana **Some ethical considerations in the development of psychopharmacological research and practice.** Progress in Neuro-Psychopharmacology. 3(1-3):133-136, 1979.

The future role of communications in psychopharmacological research and clinical practice is described, and suggestions for improving the efficiency of current communications systems in psychopharmacology are offered. Improvement of information accessibility for auxiliary medical personnel, medical personnel, and for basic researchers is urged. The International Reference Centre for Information on Psychotropic Drugs is discussed with reference to a weakness in its function, and corrective suggestions are offered. (Author abstract modified)

002554 Forster, E. F. B. Dept. of Psychiatry, University of Ghana Medical School, P. O. Box 4236, Accra, Ghana **Some ethical considerations in the development of psychopharmacological research and practice in the future.** Progress in Neuro-Psychopharmacology. 3(1-3):277-280, 1979.

Ethical considerations in the development of psychopharmacological research and clinical practice are reviewed, and the need for supranational control of the drug industry (research, quality, control, distribution) is emphasized. Topics discussed include: the dangers of proliferation of psychotropic drugs, the place of the patient in psychopharmacological research, the social setting and medical ethics, the rights of human subjects, informed consent, and the role of the World Health Organization in controlling the ethics of psychopharmacological research and practice. 4 references. (Author abstract modified)

002555 Foxall, Martha Jean Hammonds. University of Nebraska - Lincoln **Potential drug-drug interactions among institutionalized elderly.** (Ph.D. dissertation). Dissertation Abstracts International. 40(2):675-B, 1979. Ann Arbor, Univ. Microfilms No. 7918691, 222p., 1979.

Potential drug/drug interactions among residents of two institutions for the elderly were investigated, and the relationship between selected variables and drug/drug interaction potential was examined. Potential drug/drug interaction was defined as one of several situations identifiable in residents' drug profiles. Results include: 1) 515 drugs were prescribed for the 106 patients (between 61 and 93 years of age), 2) 77 potential drug/drug interactions were identified for 43 residents, 3) Lasix with lanoxin was the most common reported drug combination involved in potential drug/drug interactions, while diuretics were involved in potential drug/drug interactions more than any other drug class. (Journal abstract modified)

002556 Freytag, H. W.; Haas, H. Abteilung Neuropsychologie und Rehabilitation, Klinikum der Albert-Ludwigs-Universität, Hauptstrasse 5, D-7800 Freiburg i. Br., Germany /**On psychopathology of acquired toxoplasmosis. Also, a contribution to the problem of the exogenous paranoid hallucination syndrome. Zur Psychopathologie der erworbenen Toxoplasmose. Zugleich ein Beitrag zum Problem des exogenen paranoidhalluzinatorischen Syndroms.** Nervenarzt. 50(2):128-131, 1979.

Psychiatric aspects of acquired toxoplasmosis were studied, based on a serologically confirmed case of toxoplasmosis-encephalitis. The sickness started as a subacute and rather lucid paranoid hallucinatory psychosis and turned into a progressive typical symptomatic psychosis accompanied by personality dis-

order and extrapyramidal disorders. This infectious disease of the CNS is not only accompanied by a variety of neurological symptoms, but also by somewhat atypical psychotic and seemingly catatonic symptoms. The usual cortisone therapy poses the danger of activation of the excitant and can considerably aggravate the prognosis. It is recommended that Danaprim and Spiramycin be used for therapeutic purposes, under controlled conditions particularly when complications of the hematological picture occur. The therapy may often lead to remission of the syndrome. 20 references. (Author abstract modified)

002557 Fuller, Ray W. Lilly Research Laboratories, Indianapolis, IN 46206 **Pharmacology of central serotonin neurons.** Annual Review of Pharmacology and Toxicology. 20:111-127, 1980.

The present ability to intervene pharmacologically in central serotonin neuron function is reviewed. Drugs with improved potency and specificity are becoming available for pharmacologic manipulation of serotonin neurons in the brain. Both enhancement and impairment of serotonergic function can now be achieved by drugs acting through different mechanisms. These drugs are not only valuable tools for exploring functional roles of serotonin neurons, but they also have real or potential value in treating disease such as mental depression, obesity, myoclonus or other movement disorders such as Parkinson's disease and Down's syndrome, pain, hypertension, and endocrine dysfunction. Conflict behavior and other types of operant behavior, as well as sexual activity, also seem affected by serotonin neurons, as observed in animal studies. 120 references. (Author abstract modified)

002558 Fuxe, Kjell. Dept. of Histology, Karolinska Institute, S-104 01 Stockholm 60, Sweden **Dopamine receptor agonists in brain research and as therapeutic agents.** Trends in Neurosciences. 2(1):1-4, 1979.

The development and use of DA receptor agonists is discussed. Dopaminergic ergot derivatives have proven useful in understanding the role of dopaminergic mechanisms in the central nervous system and in human diseases. Studies, especially with bromocriptine, have demonstrated that DA receptor agonists can be important therapeutic tools in medicine. The endocrinologists use bromocriptine to lower prolactin secretion in various endocrinological diseases and to treat acromegalic patients. The neurologists have demonstrated that bromocriptine is a potent antiparkinsonian agent. It seems likely that among the dopaminergic ergot derivatives it will be possible to find an antiparkinsonian agent superior to L-DOPA. 15 references. (Author abstract modified)

002559 Gentili, C.; Ferrari, G. Istituto di Psichiatria Bologna, Bologna, Italy **Ethical problems in psychopharmacological research.** Progress in Neuro-Psychopharmacology. 3(1-3):287-291, 1979.

Ethical problems in psychopharmacological research are reviewed, and the formation of an international control committee is urged. It is contended that scientific research poses considerable ethical problems beside the often cited issue of informed consent. Various ethical problems present in the course of development of new psychotropic compounds are generally ignored, eventually leading to criticism of science and technology. To prevent the unethical use of science and technology, an international control committee, capable of coping with multinational powers such as the drug industry, must be formed. The committee should be supported by peripheral elective committees which grant the citizens direct participation in the administration of health. 10 references. (Author abstract modified)

002560 Gerber, N.; Thompson, R. M.; Smith, R. G.; Lynn, R. K. Dept. of Pharmacology, School of Medicine, University of

Oregon Health Sciences Center, Portland, OR 97201 Evidence for the epoxide-diol pathway in the biotransformation of mephenytoin. *Epilepsia*. 20(3):287-294, 1979.

A dihydrodiol metabolite of mephenytoin (5-dihydroxy-cyclohexadienyl)-5-ethyl-3-methylhydantoin and other monohydroxylated and dihydroxylated and N-demethylated metabolites were identified in urine from a male epileptic patient receiving therapy with mephenytoin (300mg/day). Metabolites, extracted from urine before and after enzymatic hydrolysis, were derivatized with a trimethylsilyl reagent and analyzed by combined gas chromatography and mass spectrometry. Two previously unreported metabolites were characterized and the structures of several other metabolites were confirmed. It is suggested that covalent binding of the mephenytoin epoxide to macromolecules may be an important factor in the production of adverse and sometimes fatal side-effects observed in patients receiving long-term therapy with mephenytoin. 19 references. (Author abstract modified)

002561 Gold, Mark S.; Pottash, A. L. C.; Sweeney, Donald R.; Kleber, Herbert D. Fair Oaks Hospital, 19 Prospect Street, Summit, NJ 07901 Effect of methadone dosage on clonidine detoxification efficacy. *American Journal of Psychiatry*. 137(3):375-376, 1980.

The effect of methadone maintenance dosage (15mg, 50mg, or 75mg) on clonidine detoxification efficacy was examined in 15 male members of a methadone maintenance treatment program who expressed a desire to discontinue methadone and who had previously made unsuccessful attempts at opiate detoxification. Clonidine (6 micrograms/kg) produced a rapid and significant decrease in opiate withdrawal signs and symptoms at 120 min postadministration for all three maintenance dose groups. The effects of clonidine were not significantly different for the three dosage groups. Relief of subjective distress was significant for all groups: all 15 subjects stated they were not in withdrawal 120 min after clonidine administration. There were no significant increases in opiate withdrawal symptoms after discontinuation on day 14 of the detoxification program or after intravenous naloxone administration. Insomnia and irritability were the only consistent complaints in all groups. Results indicate that clonidine is a potent treatment for opiate withdrawal, probably by virtue of its inhibitory effect on brain noradrenergic activity. 10 references.

002562 Goldberg, Ivan K. New York Psychopharmacologic Institute, New York, NY 10028 Dexamethasone suppression test as indicator of safe withdrawal of antidepressant therapy. *Lancet* No. 8164:376, 1980.

The use of the dexamethasone suppression test (DST) as an indicator of clinical course following termination of treatment (ECT or drug) is discussed. Testing involves administration of 1mg dexamethasone at 11 PM on day 1. At 9 AM on day 3 blood is analyzed, with nonsuppression defined as plasma cortisol greater than 7 mcg/dl. Using this procedure, 19 of 23 (83%) of depressed patients were nonsuppressors. In a study of eight patients who were nonsuppressors before treatment, retested before discontinuation of treatment after 1 month without symptoms, five suppressors on the second DST did not relapse within 2 months while all three nonsuppressors on the second DST showed a return of depressive symptoms. Thus, in this small series, DST appeared to be a sensitive and specific predictor of rapid relapse following discontinuation of tricyclic medication. 3 references.

002563 Goldberg, Solomon C. Medical College of Virginia, MCV Station, Box 710, Richmond, VA 23298 Drug and psycho-

social therapy in schizophrenia: current status and research needs. *Schizophrenia Bulletin*. 6(1):117-121, 1980.

The current status of research on psychopharmacological and psychosocial interventions with schizophrenic patients is assessed. The need to validate the diagnosis of schizophrenia; to reduce sample heterogeneity by defining subgroups based on meaningful response to drug treatment, long-term course, family history, and neurologic soft signs; and to characterize the subgroup of patients who do not respond to or do not require neuroleptic treatment are discussed. It is suggested that the prevalence of tardive dyskinesia be determined on a national and regional basis; that blood levels of neuroleptic drugs be used as indices of whether individual patients are receiving adequate dosages; and that questions of drug compliance and optimal duration of maintenance therapy be investigated further. Finally, it is recommended that the ways in which drug treatment and social skills training interact with each other be demonstrated. 21 references. (Author abstract modified)

002564 Gonzalez, Elizabeth Rasche. Journal of the American Medical Association, 535 North Dearborn Street, Chicago, IL 60610 Beyond tricyclics: outlook on antidepressant treatments. *Journal of the American Medical Association*. 243(15):1503-1504, 1980.

The contemporary variety of treatments for depressive conditions (including monoamine oxidase inhibitors, the tetracyclics, trazodone, hydroxytryptophan, dextroamphetamine, cognitive psychotherapy, psychodynamic insight therapies, specific treatments for situational depressions, sleep deprivation, electroconvulsive therapy, and tricyclic antidepressants) is reviewed. It is noted that tricyclic antidepressants are a very popular antidepressant therapy, but the need for closely monitoring plasma drug levels, and the possibility of idiosyncratic reactions have encouraged the search for other antidepressant therapies. Trazodone, a triazolepyridine derivative chemically unrelated to any other psychoactive drug, is cited as an antidepressant therapy which is likely to gain in popularity during the 1980s.

002565 Grow, T. J.; Tyrrell, D. A. J.; Ferrier, I. N.; Johnstone, E. C.; Macmillan, J. F.; Owens, D. G. C.; Parry, R. P. Div. of Psychiatry and Communicable Diseases, Clinical Research Centre, Harrow, Middlesex HA1 3UJ, England Virus-like particles in CSF in schizophrenia. *Lancet*. 8132:35, 1979.

The possibility that neuroleptic medication was responsible for the presence of a virus-like agent in the cerebrospinal fluid of some patients with schizophrenia and certain neurological conditions is considered. It is suggested that such a relationship does not exist since many CSF specimens from schizophrenic patients were taken before neuroleptic medication was started.

002566 Gutheil, Thomas G. 74 Fenwood Road, Boston, MA 02115 In search of true freedom: drug refusal, involuntary medication, and American Journal of Psychiatry. 137(3):327-328, 1980.

Issues in right to treatment/right to refuse treatment are briefly discussed. The courts have seen cases in which doctors have been sued for not medicating committed drug refusing patients as well as suits for medicating drug refusing patients. In a recent Massachusetts case, the issue was clearly over conflicting freedoms: freedom from nonconsensual invasion of bodily integrity or freedom from the greater slavery of psychosis. The preponderance of controversy surrounding involuntary medication has emphasized the civil rights perspective and the tension between the right to treatment and the right to refuse treatment. This legal emphasis has resulted in an imbalance which must be redressed by according equal weight to the clinical/therapeutic

realities and by considering the needs as well as the rights of the patient. 6 references.

002567 Gutheil, Thomas G.; Shapiro, Robert; St. Clair, R. Lawrence. 74 Fenwood Road, Boston, MA 02115 **Legal guardianship in drug refusal: an illusory solution.** *American Journal of Psychiatry*. 137(3):347-352, 1980.

Limitations of legal guardianship as a solution to drug refusal in psychiatric inpatients are illustrated with clinical examples and discussed. Theoretical conditions under which guardianship might be considered and the ideal criteria for guardianship procedures which would protect both the patient's right to treatment and right to refuse treatment are outlined. Guardianship imposes a number of basic clinical problems, among them: issues of contract and alliance resulting from ambiguities about the question of agency; the effects of the coercion involved in seeking guardianship if the countertransference; reinfantilizing the patient through denial of his autonomy and personal responsibility; and problems associated with the pool of potential guardians. Thus, the use of the guardianship process may result in an infringement of the patient's right to prompt and effective treatment, may not actually protect the patient's rights because of difficulties in finding a guardian who understands the complex issues involved and is able to unambiguously act in the patient's interest, often creates profound clinical problems, and is excessively costly both in monetary and manpower terms. Alternatives including the court as oncall guardian, rapid judicial competence rulings, outside psychiatric consultation, outside review board, or a combination of external and internal review, are discussed. 5 references. (Author abstract modified)

002568 Hartman, Henry Bob. Hofstra University **Psychological correlates of successful treatment of drug addicts maintained on methadone.** (Ph.D. dissertation). Dissertation Abstracts International. 40(2):917-B, 1979. Ann Arbor, Univ. Microfilms No. 7918423, 203p., 1978.

The relationship between some psychological characteristics of drug addicts and their response to methadone maintenance treatment was investigated via administration of the MMPI and Rotter's Internal-External Locus of Control Scale to 70 male drug addicts maintained on methadone for at least 6 months. It was found that there was an inverse relationship between successful treatment and scores on the hypochondriasis, hysteria, psychopathic deviance, schizophrenia, psychasthenia, hypomania, and paranoia scales of the MMPI. Significant positive relationships between successful treatment outcome and the following MMPI scales are reported: ego strength, masculinity/femininity and correction scales. (Journal abstract modified)

002569 Hicks, Robert; McCormick, Mark G. F.; Davis, John M. Dept. of Psychiatry, University of Chicago, School of Medicine, 950 East 59th Street, Chicago, IL 60637 **Psychopharmacology: the significance and insignificance of drugs: two paradigms.** *Psychiatric Clinics of North America*. 2(2):359-364, 1979.

The clinical efficacy of psychopharmacology is evaluated in relation to biological and psychological factors in mental illness, and a holistic conception of human illness is advocated. It is noted that conflict is expressed in the vast majority of clinician/patient interactions -- over the definition of the problem, the goals of treatment, the methods of treatment, and conditions of treatment and the relationship itself -- and negotiation by various strategies is essential to the resolution of the conflict. It is contended that patients cannot be well treated if they are viewed in a simplistic manner as having either a psychosocial or a biological problem. 11 references. (Author abstract modified)

002570 Hirshkowitz, Max; Thornby, John I.; Karacan, Ismet. Dept. of Psychiatry, Baylor College of Medicine, Houston, TX

77025 Sleep pharmacology and automated EEG analysis. *Psychiatric Annals*. 9(10):39-41, 45-49, 53-55, 1979.

Drug related effects on sleep are discussed in terms of sleep stage parameters. Sleep medications, medications used in treatment of psychiatric patients, recreational drugs, and camouflaged drugs that have specific application in the treatment of sleep disorders or are in widespread medical or nonmedical use are considered. In addition, the future of computer technology in polysomnographic research is discussed. Two tables are offered: one on the effects of various drugs on nocturnal EEG phasic and tonic events and sleep stage, and another on the effects of various drugs on total sleep time, number of awakenings, and sleep latency. 55 references.

002571 Hoffer, A. 3-A 2727 Quadra Street, Victoria, British Columbia V8T 4E5, Canada **Mega amino acid therapy.** *Journal of Orthomolecular Psychiatry*. 9(1):2-5, 1980.

Mega amino acid therapy in orthomolecular psychiatry is discussed. L-tryptophan is coming into increasing use in the treatment of insomnia and to a lesser extent in the treatment of depression. Preliminary studies show that it may also be useful in treating dermatological problems often found in schizophrenics. Leucine and isoleucine are involved in the etiology of pellagra and may have a role in schizophrenia and other similar conditions. Pellagrins treated with vitamin-B3 become psychotic if given leucine, but psychosis is reversed by treatment with isoleucine. In preliminary studies, 3g/day isoleucine was found to rapidly clear symptoms in a few acute outpatient schizophrenics. The combination of vitamin-B3 and isoleucine could be a potent one. A number of nonessential amino acids may also be essential if they cannot be made in the individual's body. Phenylketonuria may well be a tyrosine deficiency disease and tyrosine abnormalities may play a role in other forms of nonspecific mental retardation and learning disabilities. 1 reference.

002572 Holloway, Joan A.; Holloway, Frank A. Dept. of Psychiatry and Behavioral Sciences, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73190 **Combined effects of ethanol and stimulants on behavior and physiology.** *Neuroscience and Biobehavioral Reviews*. 3(3):137-148, 1979.

The literature concerning the physiological and behavioral effects of ethanol and stimulants is reviewed, with very few complete, well designed studies being revealed. Of 42 studies of animals and humans examined, only 8 used multiple doses and dose combinations. Studies of the interactions of ethanol with amphetamine, caffeine, and nicotine show antagonistic effects, no antagonistic effects, or potentiation. Since current data are incomplete and contradictory, no model of ethanol/stimulant interactions can be formulated to adequately predict behavioral, toxicological, or physiological consequences. 61 references. (Author abstract modified)

002573 Issacs, Bernard. Dept. of Geriatric Medicine, University of Birmingham, Queen Elizabeth Hospital, Birmingham B15 2TH, England **The evaluation of drugs in Alzheimer's disease.** *Age and Ageing*. 8(1):1-7, 1979.

The difficulties that might be associated with the clinical evaluation of drugs for treatment of Alzheimer's disease are discussed. The drugs to be evaluated must be capable of correcting the deficiency of choline acetyltransferase which occurs in the brains of patients with Alzheimer's disease. Since the major clinical feature of the disease is socially undesirable behavior, the appropriate criteria of the effectiveness of a drug are its ability to reduce such behavior and to retard the progression of the disease without causing important side-effects. For adequate assessment of a new drug with a claimed specific action in the correction of Alzheimer's disease, practitioners must reach

agreement on the topics of clinical criteria, methods of measuring behavior, standardization of cognitive tests, exploration of noncognitive means, and the predictive value of various measures in relation to the effectiveness of the drug. 14 references.

002574 Jacquet, Yasuko F. New York State Research Institute for Neurochemistry, Ward's Island, New York, NY 10035 **Beta-endorphin and ACTH -- opiate peptides with coordinated roles in the regulation of behaviour?** *Trends in Neurosciences*. 2(6):140-143, 1979.

The roles of beta-endorphin and corticotropin (ACTH) in regulation of behavior are examined. Problems in research, relating to passage through the blood-brain barrier, and techniques for resolving them are summarized. Opiate actions in the periaqueductal grey are discussed, together with endorphin and ACTH-induced behaviors. Abstinence behavior due to residual morphine is also discussed. The existence of a dual receptor mechanism is postulated, which serves to maintain biobehavioral equilibrium. It is concluded that the opiate abstinence syndrome is seen as an altered equilibrium in this dual mechanism. 9 references. (Author abstract modified)

002575 Jenner, P.; Marsden, C. D. University Department of Neurology, King's College Hospital Medical School, Denmark Hill, London SE5, England **The substituted benzamides -- a novel class of dopamine antagonists.** *Life Sciences*. 25(6):479-485, 1979.

Substituted benzamides are reviewed with particular reference to their similarities to and differences from classical neuroleptics. The biochemical evidence, like the function effects of the drugs, suggests that substituted benzamides exhibit only part of the spectrum of activity of classical neuroleptics. Several hypotheses are provided which might account for these characteristic actions. It is suggested that although the functional effects of substituted benzamide drugs resemble closely those of established neuroleptics, the mechanism by which this is brought about differs radically and may hint at some important distinction between different types of dopamine receptors in the brain. 74 references.

002576 Jeste, Dilip V.; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, Division of Special Mental Health Research, NIMH, Washington, DC **Tardive dyskinesia: a review of the treatment possibilities.** *Psychiatric Annals*. 10(1):26-27, 31-32, 37-38, 1980.

Clinically relevant aspects of the literature on treatment of tardive dyskinesia (TD) are reviewed and findings are summarized. Neuroleptics have been shown to produce significant improvement (symptom suppression) in about two thirds of all patients with TD. A number of other DA antagonists have been tried, with an overall improvement rate of a little over 50%. Cholinergic drugs (deanol, physostigmine, choline, and lecithin) have also been used, but their use is largely experimental. Benzodiazepines and other more specific GABA ergic drugs have reportedly resulted in significant improvement in a little more than half of the patients so treated. In general, there is a consensus that dopaminergic and anticholinergic drugs are of little value in treatment of TD. A number of dopamine-beta-hydroxylase inhibitors, such as fusaric acid and disulfiram, have produced significant improvement in TD, but more research is needed. Withdrawal of neuroleptics is followed by remission of symptoms, usually within 3 months, in about three eighths of patients. Nonpharmacological treatment of TD is as yet still rather limited. 26 references.

002577 Kaufman, Kenneth Roland; Katz-Garris, Lynda. Dept. of Psychiatry and the Behavioral Sciences, LAC/USC Medical Center, 1934 Hospital Place, Los Angeles, CA 90033 **Epilepsy,**

mental retardation, and anticonvulsant therapy. *American Journal of Mental Deficiency*. 84(3):256-259, 1979.

Inappropriate or inadequately documented medication for patients residing in a state institution for the mentally retarded was investigated. Within a 127 patient ward, 41 patients were treated with anticonvulsants, and of these patients, 24 had no documented indications for usage. Since serious side-effects of anticonvulsant medications have been reported in the literature, especially for mentally retarded people, it is essential not only that appropriate indications for such therapy be determined and documented, but also that continued usage be carefully monitored. 24 references. (Author abstract modified)

002578 Khan, Inayat. Division of Mental Health, World Health Organization, CH-1211 Geneva 27, Switzerland **Convention on psychotropic substances, 1971: the role and responsibilities of the World Health Organization.** *Progress in Neuro-Psychopharmacology*. 3(1-3):11-14, 1979.

The role and responsibilities of the World Health Organization (WHO) to the Convention on Psychotropic Substances, 1971, in its task of controlling psychotropic substances, are described. The Convention on Psychotropic Substances, 1971, formulated in Vienna, lays a great responsibility on the WHO to recommend to the United Nations Commission on Narcotic Drugs notifications initiated by the WHO, or by a party to the Convention, regarding international control. The duty to develop methodology and parameters which will enable classification of drugs according to the directives of the Convention on Psychotropic Substances, 1971, is noted. 5 references. (Author abstract modified)

002579 Konowal, Andrzej; Sznatke, Gunther; Alebic-Kolbah, Tanja; Kajfez, Franjo; Rendic, Slobodan; Sunjic, Vitomir. Institute of Organic Chemistry, Polish Academy of Science, Warsaw, Poland **General approach to chiroptical characterization of binding of prochiral and chiral 1,4-benzodiazepin-2-ones to human serum albumin.** *Biochemical Pharmacology*. 28(20):3109-3113, 1979.

The chiroptical characteristics of binding of prochiral and chiral 1,4-benzodiazepin-2-ones to human serum albumin are described. Circular dichroism (CD) measurements are used to describe the binding site on the benzodiazepine. CD measurements can also be applied to other similar systems of protein/ligand interaction with prochiral and chiral substrates. 24 references. (Author abstract modified)

002580 Kordon, C.; Ruberg, M. Unite 159 de Neuroendocrinologie, Centre Paul Broca, INSERM, 2 ter, rue d'Alesia, F-75014 Paris, France **Mental diseases and prolactin secretion. / Maladies mentales et secretion de prolactine.** *Encephale*. 5(2):115-120, 1979.

Recent reports suggesting that selective endocrine disturbances are often associated with mental disease, and that hormonal responses to treatment with antipsychotic drugs can be related to their clinical efficiency are presented. The importance of central monoamine neuron systems for both hormonal control and mental disease probably accounts for these correlations. Measurement of prolactin, a hormone primarily regulated by hypothalamic dopaminergic neurons, provides a useful tool which can help to define the symptomatology of schizophrenic or depressed patients, to calibrate drug therapy and to obtain advance warning of therapeutic side-effects. The hormone can also be used as an excellent index for screening dopamine agonist or antagonist properties of new drugs. 19 references. (Author abstract)

002581 Krogsgaard-Larsen, Povl; Scheel-Kruger, Jorgen; Kofod, Helmer. no address **GABA-neurotransmitters: pharmacological, biochemical, and pharmacological aspects.** New York, Academic Press, 1979. 552 p. \$55.

The proceedings of a 1979 international symposium on the role of GABA as a neurotransmitter are presented. Topics include GABA receptors and drugs, relevant clinical pathophysiology and pharmacology, and animal models. The papers focus specifically on molecular actions and metabolic regulation of GABA, as well as its functional interaction with other neurotransmitters. Information on novel GABA drugs and investigative tools in GABA research is included, along with discussion on GABA involvement in disease and therapeutics.

002582 Kurucz, Janos; Fallon, John. Box 156, Glen Oaks, NY 11004 **Dose reduction and discontinuation of antipsychotic medication.** Hospital & Community Psychiatry. 31(2):117-119, 1980.

Results of a program of dose reduction and/or discontinuation of antipsychotic medication of chronic schizophrenic inpatients of a state hospital are reported. An initial study in a 30 bed ward involved 15 chronic schizophrenics who met selection criteria of 5 years' continuous hospitalization for schizophrenia, medication not in excess of 300mg of chlorpromazine or its equivalent, and stability of condition/medication over the previous 60 days. At 6 month followup, seven patients were still off medication, and two had improved enough to be discharged. The program was later adopted throughout the hospital. An audit conducted 90 days after its implementation showed that 31% of the patients hospitalized continuously for 90 days or longer were not receiving antipsychotic medication. Such a program benefits patients by reducing the risk of tardive dyskinesia and other drug associated effects such as anhedonia, social isolation, postpsychotic depression, and impairment of cognitive, sensory, and motor functions. 9 references. (Author abstract modified)

002583 LaMendola, Walter; Zaharia, E. S.; Carver, Marge. Room 101, 414 West Becker Avenue, Willmar, MN 56201 **Reducing psychotropic drug use in an institution for the retarded.** Hospital & Community Psychiatry. 31(4):271-272, 1980.

A drug evaluation program designed to make psychotropic drug use consistent with the principles of an institution for the retarded is described. Specific principles include the idea that drug use could be reduced and behavior controlled with behavioral programming. It was felt that residents could perform as well without drugs. Finally, changes in the use of drugs could be a cooperative, interdisciplinary effort. Implementation of these principles lead to a reduction in the percentage of residents on medication at the institution from 34% to 21%. To determine the effect of the program on the development of skills by residents, a form of the Minnesota Developmental Programming System was administered to a random sample of 20 residents. Results showed a change in the direction of improved skill building. Findings stress the important relationship between disability grouping and optimal use of psychotropic drugs. 10 references.

002584 Leeds, Alice A. International Reference Center on Psychotropic Drugs, NIMH, 5600 Fishers Lane, Room 9C-14, Rockville, MD 20857 **The future of communication in psychopharmacotherapy.** Progress in Neuro-Psychopharmacology. 3(1-3):125-131, 1979.

The current status of communication in psychopharmacotherapy is reviewed, problems in international communication among professionals in the field of psychopharmacotherapy are identified, and basic requirements for future, effective communication in the field are discussed.

Topics discussed include: the World Health Organization International Reference Centers Network, other organizations providing information, publications, audiovisual communication, communication satellites, problems in international communication, language barriers, translation of research communications to practice, information transfer through training, resource persons, emergency information sources, and access and reliability of information. (Author abstract modified)

002585 Lehmann, H. E. Dept. of Psychopharmacology, Research and Training Building, McGill University, 1033 Pine Avenue West, Montreal, Quebec, Canada H3A 1A1 **Problems with ethical aspects of psychotropic drug use.** Progress in Neuro-Psychopharmacology. 3(1-3):271-275, 1979.

Ethical problems associated with psychotropic drug use are reviewed, and the activities of the World Health Association to deal with these ethical problems are described. Specific ethical issues still requiring clarification in psychopharmacological research are informed consent, the benefit/risk ratio, and the choice of placebo or standard. Peer review committees, if well chosen for their objectivity, general competence, and special expertise, are likely to be the best arbiters regarding such questions. The need for internationally coordinated efforts to mediate between political pressures and medical research and practices is emphasized. 7 references. (Author abstract modified)

002586 Lemberger, Louis. Lilly Laboratory for Clinical Research, Eli Lilly and Co, Indianapolis, IN 46202 **Potential therapeutic usefulness of marijuana.** Annual Review of Pharmacology and Toxicology. 20:151-172, 1980.

Clinical research on the therapeutic effectiveness of marijuana is reviewed and the current controversy over such drug treatments is discussed. Specific drug categories in which cannabinoids may possess therapeutic potential include their antiasthmatic, anticonvulsant, and antiemetic properties; appetite stimulation properties; effects on glaucoma; and psychopharmacologic effects (anxiety, antidepressant and sedative hypnotic). Miscellaneous uses include use as an antitumor agent and in the treatment of hypertension. The research to date indicates problems with respect to reproducible absorption and production of consistent and predictable pharmacologic effects with delta 9-THC, the active marijuana constituent. Synthetic cannabinoid derivatives have been developed; however, some of these are crystalline, readily absorbed, and capable of producing reproducible effects. They also possess a greater degree of organ specificity and selectivity in their actions. 110 references.

002587 Leon, Carlos A. Unidad de Salud Mental, Hospital Universitario, Cali, Colombia **Ethical aspects of psychopharmacology.** Progress in Neuro-Psychopharmacology. 3(1-3):297-301, 1979.

Ethical aspects of psychopharmacology are discussed in relation to the principles contained in the Declaration of Hawaii (1978). Ethical implications of the following topics are discussed: 1) psychopharmacological research in human Ss with special emphasis on the use of placebo for drug trials and problems related to the choice of research methods; 2) prescription of psychotropic drugs, the role of physicians, and the problem of the delegation of functions to paramedical personnel; 3) the administration of psychotropic drugs -- informed consent, side-effects, and groups at special risks; 4) availability and cost of drugs, generic and trade name preparations, as well as selective use of drugs for different populations. 7 references. (Author abstract modified)

002588 Liebowitz, Michael R.; Klein, Donald F. Dept. of Clinical Psychiatry, College of Physicians and Surgeons, Co-

lumbia University, New York, NY 10032 **Hysteroid dysphoria.** *Psychiatric Clinics of North America.* 2(3):555-575, 1979.

Diagnostic criteria for hysteroid dysphoria and its psychopharmacologic management are examined. Evidence is presented for the effectiveness of monoamine inhibitors with this small group of characterologically disturbed atypical depressives, most of whom are women. A combination of inhibitors and psychotherapy is useful in the initial treatment phase while inhibitors may be withdrawn later in treatment if gains are made in social adjustment. The syndrome also overlaps with cyclothymic bipolar mood disorder, and research is needed to elucidate the nosological boundaries of the various life long or intermittent affective disorders that manifest clinically because of characterologic difficulties. 45 references.

002589 Lin, Ih Foo; Spiga, Ralph; Fortsch, William. Tinley Park Mental Health Center, 7400 West 183rd Street, Tinley Park, IL 60477 **Insight and adherence to medication in chronic schizophrenics.** *Journal of Clinical Psychiatry.* 40(10):430-432, 1979.

The relationship between insight and perceived benefits from medication in patients and psychopharmacotherapeutic compliance was investigated in a sample of chronic schizophrenics. Those patients who had insight, perceived benefits from medication, and also perceived a relation between the two were more likely to take medication than those who did not have insight or perceive benefits. A speculative model and possible methods of increasing medication adherence are suggested. 7 references. (Author abstract modified)

002590 Lyman, Gary H.; Williams, Charles C.; Preston, Dennis. University of South Florida College of Medicine, 12901 North 30th Street, Tampa, FL 33612 **The use of the lithium carbonate to reduce infection and leukopenia during systemic chemotherapy.** *New England Journal of Medicine.* 302(5):257-260, 1980.

In an investigation of the lithium carbonate effects on infectious complications accompanying systemic chemotherapy, 20 patients with small cell bronchogenic carcinoma receiving combination chemotherapy and radiation therapy were administered lithium carbonate. Matched controls (n=25) received no additional therapy. Controls experienced more days with neutropenia than experimentals (2.17 days per 100 patient days vs 29), more severe febrile episodes (seven patients vs one), more days hospitalized with fever and neutropenia (1.92 vs 18 per 100 patient days), and more infection related deaths (five vs none). Infection free survival was significantly longer in lithium treated patients than in controls. Delay in subsequent chemotherapy was longer and the number of dose reductions was greater in controls. For both leukocytes and neutrophils, the first cycle nadir, mean of all treatment nadirs, and lowest nadir observed during treatment were significantly higher in the lithium group. Mean midcycle monocyte counts were greater in the lithium group, and correlated with concurrent serum lithium levels. 21 references. (Author abstract)

002591 Margules, David L. Dept. of Psychology, Temple University, Philadelphia, PA 19122 **Beta-endorphin and endoloxone: hormones of the autonomic nervous system for the conservation or expenditure of bodily resources and energy in anticipation of famine or feast.** *Neuroscience and Biobehavioral Reviews.* 3(3):155-162, 1979.

It is postulated that the autonomic nervous system contains two divisions that direct the conservation or expenditure of bodily resources and energy in anticipation of nutrient shortage or excess in the environment. The endorphinergic division uses opioid peptides to convey the message of expected shortage and

stimulate the organism to build up stores for impending famine by increasing inflows and decreasing outflows. The endoloxinergic division uses endogenous naloxone-like substances to decrease inflows and increase outflows. The integrated and widespread actions of these system may influence almost every tissue in the body. 46 references. (Author abstract modified)

002592 Marsden, C. D.; Jenner, P. University Dept. of Neurology, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, England **The pathophysiology of extrapyramidal side-effects of neuroleptic drugs.** *Psychological Medicine.* 10(1):55-72, 1980.

The mechanisms responsible for the production of major extrapyramidal side-effects (parkinsonism, akathisia, dystonic reactions, chronic tardive dyskinesia) are reviewed in the light of the complex effects of neuroleptics on cerebral dopamine (DA) systems. Drug-induced parkinsonism is held to be due to postsynaptic DA receptor blockade in the striatum, while akathisia may be due to a similar blockade of DA receptors in mesocortical areas. Acute dystonic reactions appear to be due to the interaction between the development of postsynaptic DA receptor supersensitivity with increased DA turnover and release provoked by acute administration of these drugs. Chronic tardive dyskinesias appear to result from a gradual disappearance of DA receptor blockade in the striatum by neuroleptic drugs and the emergence of striatal DA receptor supersensitivity, despite continuation of drug intake. Similar tolerance in mesolimbic areas may occur, casting doubt on the general hypothesis that the therapeutic antipsychotic effect of these drugs is due to their ability to block DA receptors. 149 references. (Author abstract modified)

002593 Marshall, Barringer D., Jr.; Wallace, Charles J.; Liberman, Robert Paul. Camarillo State Hospital-UCLA Neuropsychiatric Institute, Box A, Camarillo, CA 93010 **Assessing psychiatric patients' compliance in taking medication.** *Hospital & Community Psychiatry.* 30(11):788, 1979.

Seven patients were evaluated for their compliance with the administration of an inactive protein placebo. Five of the patients were low functioning chronic schizophrenics, one had pathological obesity, and one was diagnosed as having chronic nonpsychotic organic brain syndrome secondary to trauma. The study attempted to develop interventions that would motivate patients to take their medications regularly and independently. Results suggest that the reinforcement of drug compliance may be less effective than the powerful stimulus control provided by attendance at meals and the presence of individual pill bottles.

002594 Marshall, John B.; True, A. C. University of Nebraska Medical Center, Omaha, NE 68101 **Ads for tricyclic antidepressants: how much is enough?** *New England Journal of Medicine.* 301(9):502-503, 1979.

An advertisement recently run in medical journals for amitriptyline (Elavil) is criticized in a letter to the editor. The advertisement depicts a bottle containing 100 75mg tablets. Thus the depressed recipient would receive 7500mg, clearly a quantity that if taken in a suicidal overdose could prove fatal. It is concluded that the advertisement is misleading and potentially harmful. In a reply by Merck, Sharpe & Dohme's vice president of medical services, the need to carefully limit and monitor prescriptions for tricyclics is reiterated. It is noted that the advertisement in question showed the actual trade package in which the medication is delivered to the pharmacist and from which individual prescriptions would be filled. 3 references.

002595 McLean, Peter D.; Hakstian, A. Ralph. Dept. of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Clinical depression: comparative effi-**

cacy of outpatient treatments. *Journal of Counseling and Clinical Psychology.* 47(5):818-836, 1979.

The efficacy of psychotherapy, behavior therapy, amitriptyline, and relaxation training for clinical depression was investigated in order to consolidate the findings of previous studies. One hundred seventy-eight moderately clinically depressed clients were given 10 weeks of psychotherapy, behavior therapy, drug therapy, or relaxation therapy (treatment control condition). Fifty-five normal subjects were evaluated for comparison purposes, but were not part of the data analyses. In addition to showing differential treatment drop out rates, results showed behavior therapy to be superior on 9 of 10 measures at the end of treatment and marginally superior at the 3 month followup. Psychotherapy performed most poorly on most outcome measures at both evaluation periods, and there were no significant differences between drug therapy and relaxation therapy on any outcome measure. Neither therapist experience nor client cluster type interacted with treatment. There was an overall significant difference between high and low treatment responders, but discriminant function classification predicted treatment responses correctly in only 68% of the cases. It is concluded that five characteristics of behavior therapy are conducive to recovery from clinical depression: 1) high treatment structure, 2) social learning rather than disease model rationale, 3) goal attainment focus, 4) externalized interests, and 5) social prophylaxis. 33 references. (Author abstract modified)

002596 Mendlewicz, J. Dept. of Psychiatry, Erasme Hospital, University of Brussels, Route de Lennik 808, B-1070 Brussels, Belgium **Perspectives and practical applications in psychopharmacogenetics.** *Progress in Neuro-Psychopharmacology.* 3(1-3):155-163, 1979.

The interaction between genetic and environmental factors affecting drug metabolism in humans is discussed in relation to attempts to understand therapeutic response in psychopharmacology. The relationship between genetics and environmental factors is illustrated for various psychotropic drugs, such as the monoamine oxidase inhibitors (MAOI), tricyclic drugs, and lithium salts, as well as for enzymes involved in the synthesis and degradation of biogenic amines. New perspectives in pharmacogenetics and their relevance to psychopharmacology are discussed. 22 references. (Author abstract modified)

002597 Mosher, Loren R.; Meltzer, Herbert Y. Center for Studies of Schizophrenia, Clinical Research Branch, NIMH 5600 Fishers Lane, Room 10-95, Rockville, MD 20857 **Drugs and psychosocial treatment: editors' introduction.** *Schizophrenia Bulletin.* 6(1):8-9, 1980.

The importance of combining psychosocial treatment with neuroleptic drug treatment of psychosis, particularly schizophrenia, is discussed. A tendency was demonstrated in the last two decades to conceive of neuroleptic treatment as the only proven form of treatment for psychosis. The factors which further contributed to the diminution of the relative importance of psychosocial treatments of psychosis are identified. However, after 25 years of experience with neuroleptics as antipsychotic drugs, their limitations, such as the appearance of tardive dyskinesia, have become apparent. It can now be argued that the comprehensiveness of the psychosocial treatment program and the availability of a social network to reinforce, maintain, and support the gains achieved by more formal treatment programs, of which psychopharmacology may be an essential element, appear to be critical.

002598 Moyer, Phillip C.; Hysler, Susan R. Trinity University, San Antonio, TX 78212 **Children on drug therapy: counselors can**

help. *Elementary School Guidance and Counseling.* 14(3):196-204, 1980.

Guidelines for providing counseling services to children experiencing health problems requiring drug therapy are reviewed. These services include: 1) identifying special needs of specific children, their families and teachers; 2) providing psychological and technical support for children, families, and teachers; and 3) promoting school responsiveness to the health problems and needs of individual pupils. The counselor must act to promote self-awareness and self-development among these students, and effective techniques include individual and group counseling with children, consultation with teachers and parents, and conferences involving various combinations of the above groups. A case study is included to demonstrate how the counselor can help the child and significant others cope with the demands of the health condition and accompanying drug therapy. 5 references.

002599 no author. no address **International Symposium on GABA and other Inhibitory Neurotransmitters.** *Brain Research Bulletin.* 4(5):683-714, 1979.

Abstracts are presented of 165 papers read at the International Symposium on GABA and other Inhibitory Neurotransmitters, held November 1979 in Myrtle Beach, South Carolina. An index to participants (with abstract numbers) is included.

002600 no author. no address **Prisoner receives \$518,000 settlement in suit for improper administration of psychotropic drugs.** *Mental Disability Law Reporter.* 3(3):189, 1979.

An out of court settlement was awarded in the case of Tucker V. Hutto to a prison inmate who suffered paralysis from improper administration of psychotropic drugs which were given to him without his consent. The inmate alleged that he was administered Prolixin and Stelazine by prisoners and other untrained personnel in excessive doses. After paralysis set in the prisoner alleged his condition deteriorated further through neglect. The defendants, a prison and a state mental hospital, agreed to pay \$518,000 if claims against them were dropped.

002601 no author. no address **Rennie v. Klein.** *Law & Behavior.* 4(3):2-8, 1979.

The court decision in Rennie v. Klein, regarding the right to refuse treatment with behavior modifying medication, is reviewed and excerpts are presented. The plaintiff sought to enjoin the defendant psychiatrists and officials at Ancora Psychiatric Hospital from forcibly administering drugs to him in the absence of an emergency. In excerpts from the decision, issues relating constitutional rights (cruel and unusual punishment, freedom of expression, due process, and privacy rights) are considered within the context of legal precedents. Since the involuntary administration of prolixin was terminated, the court issued no injunction. However, the court will immediately schedule further hearings should Ancora doctors seek again to administer drugs to Rennie against his will in nonemergencies.

002602 no author. no address **Doctor negligent for prescribing Valium to patient without checking psychiatric history.** *Mental Disability Law Reporter.* 3(4):249-250, 1979.

A decision by a trial court, involving negligence in the prescribing of valium, has been upheld as not clearly erroneous by the Fifth Circuit Court. The higher court agreed that a military doctor acted negligently in prescribing a 50 day supply of Valium to a serviceman without first taking an adequate history or checking psychiatric records. It agreed that the doctor's omission was a proximate cause of a car collision involving the serviceman, even though the driver had enough alcohol in his blood following the accident to be legally intoxicated.

002603 no author. no address **Treatments for agoraphobia.** *Lancet*. No. 8144:679-680, 1979.

Behavioral and pharmacologic treatments for agoraphobia are reviewed, and contributions to management of agoraphobia which general practitioners can make are discussed. Behavioral approaches to treatment have generally focused on persuading the patient to remain in the phobic situation for long periods until the discomfort dies down. Large doses of sedatives such as benzodiazepines or alcohol are counterproductive and seem to reduce the efficacy of exposure treatment, whereas antidepressants do not reduce the efficacy of exposure treatment yet deal with the tendency toward depressive moods noted in agoraphobic patients. A simple manual for general practitioners which explains the principles of exposure treatment (Marks, 1978) is noted. 32 references.

002604 no author. no address **America salutes lithium.** *Lancet*. No. 8153:1168, 1979.

The use of lithium for patients with different types of affective disorders is discussed. The available literature is reviewed. There is agreement that lithium is the treatment of choice for all but highly overactive or atypical manics, and that lithium has value in the prophylaxis of bipolar affective disorder. It is in relation to the efficacy of lithium in the prophylaxis of ordinary unipolar depression that dissent begins to appear. The more closely a patient fits the bipolar stereotype, the better the chance of a good response to lithium. It is concluded that decisions about lithium prophylaxis should be influenced by all potentially predictive indicators, by the seriousness of the condition, and by the risks and benefits of alternative treatments. 3 references.

002605 no author. no address **FDA advisers give green light to new minor tranquilizer.** *Medical World News*. 20(24):36, 1979.

The approval of alprazolam, a new benzodiazepine, by the FDA is reported. Alprazolam is recommended for treatment of anxiety with or without depression. Testimony from Upjohn stated that double-blind clinical trials had been conducted which demonstrated fewer side-effects than diazepam. The clinical trials, involving psychiatric outpatients with high anxiety levels, showed that alprazolam was also more effective than diazepam in regard to overall patient condition and anxiety ratings. Opponents of the approval of new tranquilizers argue that they relieve symptoms but do not aid patients in resolving underlying problems.

002606 no author. no address **Federal court issues most encompassing right to refuse treatment standards to date.** *Mental Disability Law Reporter*. 4(1):11-14, 1980.

A recent federal court decision in Massachusetts supporting the constitutional right of voluntary and involuntary mental patients to refuse medication except when there exists an emergency that would bring about a substantial likelihood of physical harm to the patient or others, is reviewed. The court also upheld, on statutory grounds, a similar right to object to seclusion when there is no emergency. On the basis of violations of both the rights to refuse medication and to avoid forcible seclusion, the court enjoined the staff of Boston State Hospital from contravening those rights, but refused to award the plaintiffs monetary damages since the staff had acted in good faith given the state of the law and the trying circumstances that existed in 1973, when the incidents took place. (Author abstract modified)

002607 no author. no address **Colorado Supreme Court rules that without prior adjudication a patient may refuse treatment.** *Mental Disability Law Reporter*. 4(1):34, 1980.

The recent ruling of a Colorado Supreme Court that a mental patient cannot be forced to undergo treatment with drugs having serious deleterious side-effects unless a competent tribunal has judged that the patient's illness has so impaired his judgment that he is incapable of participating in decisions affecting his health, is reviewed. The court reached a decision based on Colorado law and thus did not consider constitutional issues. A peripheral issue concerned the appellant's right as an indigent to be provided with a trial transcript of a mental health proceeding at state expense, was also addressed by the court.

002608 no author. no address **First Circuit limits liability of agency administration for improper medication of patient.** *Mental Disability Law Reporter*. 4(1):40, 1980.

A recent first circuit court decision affirming a district court ruling that the director of the Rhode Island Department of Mental Health, Retardation, and Hospitals could not be held liable for monetary damages nor enjoined for medication improperly dispensed to a patient at one of the state facilities under his authority is reviewed. The court ruled that damages would require a showing that the director had a role in administering the harmful drugs, and that an injunction would have to be based on a showing that the director either was involved in the drug's administration to the patient or had approved an unlawful policy that caused the harm. The case arises out of the repeated administration of phenothiazines to a moderately retarded juvenile suffering from childhood schizophrenia who manifested allergic reactions to that family of drugs.

002609 Norman, Trevor R.; Burrows, Graham D.; Scoggins, Bruce A.; Davies, Brian. Dept. of Psychiatry, Clinical Sciences Building, Royal Melbourne Hospital, Victoria 3050, Australia **Pharmacokinetics and plasma levels of antidepressants in the elderly.** *Medical Journal of Australia*. 1(7):273-274, 1979.

Drug metabolism and pharmacokinetics in the elderly are discussed. Potentially the aging process can affect absorption, distribution, metabolism, or excretion of drugs to bring about observed pharmacokinetic and pharmacodynamic changes. Each of these possibly affected functions is discussed more fully. The literature on tricyclic antidepressant plasma levels and age is briefly reviewed. It is concluded that pharmacokinetics and steady state plasma levels of tricyclic antidepressants are likely to be altered in the elderly. More systematic studies are required to evaluate this effect in both elderly patients and elderly volunteers. 26 references.

002610 O'Leary, K. Daniel. Dept. of Psychology, State University of New York, Stony Brook, Long Island, NY 11794 **Pills or skills for hyperactive children.** *Journal of Applied Behavior Analysis*. 13(1):191-204, 1980.

The controversial nature of drug treatment of hyperactivity, the incidence and sequelae of hyperactivity, and problems of differential diagnosis of hyperactivity versus aggression are discussed. The effects of psychostimulant medication and behavior therapy on hyperactive children are reviewed with regard to effects on their social and academic behavior. Both treatments have resulted in clear short-term changes in social behavior but neither long-term academic nor long-term social effects have been shown with either treatment. Short-term effects on academic behavior have resulted from behavioral interventions but not from psychostimulants. However, the interventions have been too brief to allow one to draw unequivocal conclusions about the clinical efficacy of behavioral treatments. Although there have been long-term evaluations of psychostimulant therapy, there have not been any evaluations of long-term behavioral treatment programs for hyperactive children. Given the salutary short-term effects of behavior therapy with hyperactive

children, extended clinical trials of behavior therapy are recommended. 68 references. (Author abstract modified)

002611 Olatawura, M. O. Dept. of Psychiatry, University College Hospital, Ibadan, Nigeria **Perspectives in the treatment of mental disorders in developing countries: Africa.** Progress in Neuro-Psychopharmacology. 3(1-3):119-123, 1979.

The treatment of mental disorders in developing countries in Africa is reviewed. It is noted that, in general, traditional forms of treatment coexist with modern medical treatment of mental disorders. None of the few reports of clinical trials from different parts of Africa have taken into account the variations in the clinical presentation of mental disorders, the nutritional status, and general physical health of African patient populations, in their discussions of the effectiveness of psychotropic agents. Research into traditional forms of treatment and the effectiveness of psychotropic agents in populations in different states of general health and nutrition is viewed as a priority activity. 11 references. (Author abstract modified)

002612 Opler, Lewis A.; Katz, Ira; Kobayashi, Joyce; Ruiz, Pedro. Bronx Psychiatric Center, 1500 Waters Place, Bronx, NY 10461 **Tardive dyskinesia and institutional practice: current issues and guidelines.** Hospital & Community Psychiatry. 31(4):239-245, 1980.

Some of the relevant literature on tardive dyskinesia is reviewed focusing on pragmatic questions for practicing psychiatrists. The situations where alternatives to neuroleptic treatment should be considered are identified. The alternatives to the existing health delivery options required to allow a realistic response to the problems posed by tardive dyskinesia are discussed. New areas of research aimed at preventing and treating tardive dyskinesia are described. 41 references.

002613 Osuntokun, B. O. Neurology Unit, Dept. of Medicine, University of Ibadan, Ibadan, Nigeria **Treatment of epilepsy: with special reference to developing countries.** Progress in Neuro-Psychopharmacology. 3(1-3):81-94, 1979.

The need for accurate diagnosis in epilepsy is discussed in relation to difficulties encountered in the treatment of epilepsy in developing countries. It is recommended that pharmacotherapy be as simple as possible, and economic and availability factors in selecting the drugs of choice for treating epilepsy in the developing nations are discussed. Grand mal and focal epilepsies can be controlled by phenobarbitone, with phenytoin, sulthiame, and carbamazepine kept as reserves or adjuncts. Minor (generalized) epilepsies can be controlled by ethosuximide, with clonazepam and sodium valproate (sodium dipropylacetate) as reserve drugs and adjuncts. For status epilepticus, diazepam is effective and readily available, with clonazepam and phenytoin as alternatives. Problems and solutions to problems in the management of epilepsy in the developing countries are discussed. 55 references. (Author abstract modified)

002614 Pare, C. M. B. Dept. of Psychological Medicine, St. Bartholomew's Hospital, West Smithfield, London EC1A 7BE, England **Monoamine oxidase inhibitors in resistant depression.** International Pharmacopsychiatry. 14(2):101-109, 1979.

The effectiveness of monoamine oxidase inhibitors (MAOI) in treating therapy resistant depression is discussed. It is contended that the MAOIs are effective in atypical cases where they are useless in treatable depressions, and that patients responding to MAOI treatment differ as a group from the common endogenous depressive disorders. Comments are made on recommended dosage, clinical usage of the MAOIs, and techniques which combine MAOI treatment with the antidepressant drugs. 38 references.

002615 Persson, Goran. Dept. of Psychiatry, Sahlgren's Hospital, S-413 45 Gothenburg, Sweden **Factors related to drug compliance and attrition in neurotic outpatients treated with anxiolytics.** Acta Psychiatrica Scandinavica. 60(2):163-169, 1979.

Forty-six outpatients with anxiety tension states took part in a study on the effects of anxiolytic drugs. Based upon followup examination, three groups were formed: completers, who did not experience side-effects to be of such intensity that they changed the recommended dose; deviators, who due to side-effects changed the recommended dose temporarily or permanently; and attritors who dropped out due to side-effects or insufficient drug effect. Completers, deviators and attritors were similar with regard to age, education and social class. They were also similar with regard to initial distress level. Completers had the highest scores on scales measuring the personality traits defence of status and guilt feelings and on the factor index neurotic self-assertiveness, while attritors had the lowest scores. Completers, deviators and attritors were similar with regard to experience of the first consultation. Patients with a more favorable experience of the first consultation reported taking lower doses of the drugs. 18 references. (Author abstract modified)

002616 Pohl, Richard Wilson. University of Minnesota **Adventitious taste aversion conditioning: contaminant of psychopharmacological research.** (Ph.D. dissertation). Dissertation Abstracts International. 39(9):4640-B, 1979. Ann Arbor, Univ. Microfilms No. 7906365, 130p., 1978.

The possibility that pCPA alcohol experiments are contaminated by taste aversion conditioning is evaluated on the basis of three lines of evidence. These comprise a consideration of the design used to examine the effects of pCPA on alcohol drinking, the results of pCPA alcohol experiments, and direct experimental evidence. It is concluded on the basis of these experiments that taste aversions conditioned by pCPA depend on the temporal relations between pCPA and alcohol, and are not dependent on any intrinsic property of pCPA, of alcohol, or of saccharin. (Journal abstract modified)

002617 Porter, Ruth. Ciba Foundation, 41, Portland Place, London W1N 4BN, England **Report on a symposium on monitoring drug concentrations in neuropsychiatry, London, July 3-5, 1979.** European Journal of Clinical Pharmacology. 17(3):231-232, 1980.

A position paper on monitoring plasma concentrations of various classes of psychotropic drugs, which was adopted at a Ciba Foundation symposium in London during July 1979, is presented. Pros and cons of monitoring plasma concentrations of anticonvulsant drugs, tricyclic antidepressants, lithium, neuroleptics, monoamine oxidase inhibitors, and benzodiazepines are discussed. It is noted that the overlap of therapeutic and toxic concentrations demands the application of clinical judgment in assessing a given drug level in a given patient. The utility of monitoring plasma concentrations to assess patient compliance is noted.

002618 Post, Robert M. Section on Psychobiology, Biological Psychiatry Branch, NIMH Building 10, Room 3S239, Bethesda, MD 20205 **Intermittent versus continuous stimulation: effect of time interval on the development of sensitization or tolerance.** Life Sciences. 26(16):1275-1282, 1980.

The experimental literature on the effect of time interval between repeated application of stimuli or drugs on the development of sensitization or tolerance is reviewed. It is noted that studies from several disciplines support the concept that the temporal characteristics of repeated drug, electrophysiological, or psychological stimuli can affect the direction of cellular and behavioral adaptation. While chronic, continuous stimulation is

often associated with the development of tolerance, intermittent stimulation, under some circumstances, may have the opposite effect and be associated with sensitization or reverse tolerance. While many other variables can affect the development of sensitization or tolerance, it is suggested that the interval between electrical, drug, or psychological stimuli is important in determining subsequent responsivity. Temporal characteristics should be carefully considered both in relation to experimental design and theoretical implications; they may shed light on similarities and differences in mechanisms underlying tolerance and sensitization. 68 references. (Author abstract modified)

002619 Post, Robert M.; Cutler, Neal R. Section on Psychobiology, Biological Psychiatry Branch, NIMH, Bldg. 10, Rm. 35239, 9000 Rockville Pike, Bethesda, MD 20205 *The pharmacology of acute mania. (Unpublished paper).* Bethesda, MD, NIMH, 1979. 80 p.

The pharmacology of the acute manic syndrome is reviewed from the point of view of conventional and experimental therapeutics. The clinical efficacy of various pharmacological agents is briefly discussed. Primary emphasis is placed on the theoretical implications of the mechanisms of action of drugs in order to explore the pathophysiology of the acute manic process. Biochemical theories of mania derived from the use of relatively specific pharmacological agents are reviewed. Several agents are shown to be clinically effective in the treatment of the manic syndrome and other experimental agents provide hints to the underlying biology of mania. Most of the acutely acting anti-manic agents which also exacerbate the depressive process appear to be acting primarily through the catecholamine system. Similarly and reciprocally, many of the useful antidepressant agents which have apparent effects on noradrenergic and perhaps serotonergic metabolism may also be associated with an increased incidence and exacerbation of mania. To the extent that the preliminary data suggest that different patients may respond to lithium, carbamazepine, or to neuroleptics, issues of biology and pharmacological heterogeneity in the manic syndrome are highlighted. Suggestions for future approaches to the investigation of the pharmacology of the acute manic syndrome are given. 175 references.

002620 Post, Robert M.; Jimerson, D. C.; Bunney, W. E., Jr. Building 10, Room 35239, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 *Perspectives in the treatment of the psychoneurological disorders: affective disorders.* Progress in Neuro-Psychopharmacology. 3(1-3):65-74, 1979.

Current research strategies in the pharmacotherapy of the affective disorders are reviewed in an attempt to highlight major trends and areas of particular promise. There has been some progress toward the identification of biologically defined subgroups by assessing amine metabolites in urine or cerebrospinal fluid which may lead to a more rational choice of therapies for depressed patients. The use of drugs with receptor agonist properties may help define biological substrates altered in affective illness and lead to new approaches in treatment, such as utilization of low doses of receptor agonists which may preferentially stimulate presynaptic receptors. Study of time dependent and adaptive changes in receptor sensitivity may also add an important perspective in conceptualizing the cyclic process in manic-depressive illness and its treatment. 82 references. (Author abstract modified)

002621 Prien, Robert F. NIMH, 5600 Fishers Lane, Rockville, MD 20875 *Problems and practices in geriatric psychopharmacology.* Psychosomatics. 21(3):213, 217, 221-223, 1980.

Special problems encountered in the use of psychopharmacologic agents for geriatric patients are reviewed. These problems

include the presence of multiple medical conditions, use of multiple drug regimens, altered physiologic responses, diagnostic problems, and noncompliance. The findings of nine major surveys of prescription drug use conducted within the past decade as they apply to the use of psychotropics by the elderly are reviewed. It is concluded that older patients account for a significant proportion of the psychopharmacologic market. Sedatives and hypnotics appear to be the most disproportionately issued to the elderly. 21 references (Author abstract modified)

002622 Quattlebaum, Judith H. National Committee on the Treatment of Intractable Pain, P.O. 34571, Washington, DC 20034 */The campaign to provide all effective drugs and methods in the treatment of intractable pain./ Campaign against pain.* Archives of the Foundation of Thanatology. 7(3):92, 1979.

A summary of a paper read at a symposium on the Child and Death, held in New York City, January 1979, is presented. The campaign of the National Committee on the Treatment of Intractable Pain is described. The goal of the Committee is to sweep away bureaucratic obstructions, popular ignorance, and professional resistances to providing all effective drugs and methods in the treatment of pain, including the availability of heroin, for patients who suffer from pain in advanced cancer. The nonavailability of heroin, for political not medical reasons, is given as a prime example of what is wrong with current attitudes toward the use of narcotics for pain. The use of heroin for relief of severe, acute pain in other countries such as Great Britain is discussed. The fact that no two analgesics have entirely identical properties or produce the same effects on individual patients is seen as justification for having a variety of alternative drugs available, including heroin. (Journal abstract modified)

002623 Rafaelsen, Ole J. Dept. of Psychiatry, Rigshospitalet 9, Blegdamsvej, DK-2100 Copenhagen O, Denmark *Ethics of psychopharmacological research.* Progress in Neuro-Psychopharmacology. 3(1-3):281-285, 1979.

In a review of ethical aspects of psychopharmacological research, it is contended that it is unethical not to undertake research in psychopharmacology while thousands suffer from mental disorders, and it is unethical not to apply proper research principles to obtain maximal information from the observations of patients treated by different drugs or techniques. The principles of the Helsinki Declaration of 1964 are noted. The following are described as the aims of ethical research in psychopharmacology: 1) description of spontaneous history, description of diagnostic and therapeutic techniques and processes, description of goals, description of results (including treatment failures), and use of prospective rather than retrospective studies. 11 references. (Author abstract modified)

002624 Rastogi, R. B.; Ling, G. M. Dept. of Psychiatry, McGill University, Montreal, Quebec, Canada *Behavioural hyperactivity of children and therapy with C.N.S. stimulants.* Totus Homo. 9(1-2-3):83-88, 1979.

Behavioral hyperactivity of children is conceived as a medicosocial problem which may involve neurological components as well as social and environmental factors, and therapy for hyperactivity children with CNS stimulants is reviewed. Hypothesized neurochemical abnormalities underlying hyperactivity or hyperkinesis are reviewed, and the relationships among behavioral hyperactivity, minimal brain dysfunction, and learning disability are discussed. Even though stimulant drugs offer a modality of treatment for the short-term management of hyperkinetic children, they do not provide the necessary influences to alter later social and academic adjustment. Furthermore, adverse effects associated with the use of stimulants raise the question of the most rational use in this condition. The risk of drug

dependency as a consequence of therapy with CNS stimulants is discussed. 25 references.

002625 Raynes, Norma V. General Practice Research Unit, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, England **Factors affecting the prescribing of psychotropic drugs in general practice consultations.** *Psychological Medicine*. 9(4):671-679, 1979.

The characteristics of patients and information gathering processes in general practice consultations producing prescriptions for antibiotics and psychotropic drugs are discussed. The contribution of patients presenting symptoms and the exploration of these by the general practitioner in the prescribing of psychotropic drugs are compared with the contribution made by diagnosis. 28 references. (Author abstract modified)

002626 Reifman, Ann; Wyatt, Richard Jed. Saint Elizabeths Hospital, William A. White Building, Room 536, Washington, DC 20032 **Lithium: a brake in the rising cost of mental illness.** *Archives of General Psychiatry*. 37(4):385-388, 1980.

An estimate of the cost of care for manic-depression before lithium was introduced is compared with cost estimates after lithium in order to compute the economic impact of its success on the United States. Economic gains in production are also calculated. It is suggested that assumptions and exclusions err on the conservative side so that estimates, if inaccurate, are low. It is claimed that the use of lithium as a treatment for manic-depression has saved \$2.88 billion in 10 years and resulted in a \$1.28 billion gain in production, or a conservative total of over \$4 billion. 11 references. (Author abstract modified)

002627 Roizin, Leon; Shiraki, Hirotosuga; Grcevic, Nenad. Division of Pathology, Columbia University, New York, NY 10027 **Neurotoxicology.** New York, Raven, 1977. 658 p. Vol.1 \$63.00.

Clinical, biochemical, pharmacologic, toxicologic, genetic, and teratogenic effects of a series of drugs and neurotoxic agents found in the environment are described. Food/drug and alcohol/drug interactions are described. The effect of alcoholism on the nervous system, and the significance of vitamin B deficiency in this state are discussed. The significance of the blood/brain barrier and of the multiple factors in the production of the resulting lesions is emphasized. The significance of the relationship of abnormal functions to structure is presented. It is concluded that side-effects may be masked, toxic effects are usually temporary, many drugs affect numerous sites and have many side-effects, biological events are complex, and adverse results may be the result of multiple normal and extraneural factors.

002628 Rotshenker, S. no address **44th Meeting of the Israel Physiological and Pharmacological Society.** *Israel Journal of Medical Sciences*. 15(11):946-956, 1979.

Abstracts of papers presented at the 44th meeting of the Israel Physiological and Pharmacological Society are presented. Topics include the animal and human tissue preparations used in drug research, prolactin releasing activity phenytoin pharmacokinetics, research on brain adenylate cyclase complex, noradrenergic and serotonin activity in neuronal research, the photoreceptor transduction process, humoral endorphin as a neurohormone in opiate activity, the effects of alcohol on photoreceptor response, biochemical and electrophysiological aspects of the insect sensory system, the effect of pH changes on acetylcholine receptors, and physiological and biochemical aspects of exercise and acclimatization.

002629 Salzman, Carl. Psychopharmacology Research Laboratory, Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Update on geriatric psychopharmacology.** *Geriatrics*. 34(8):87-90, 1979.

Recent findings in the area of geriatric psychopharmacology are reviewed. The relationship between age and steady state plasma levels of tricyclic antidepressants is discussed, including decreased hepatic metabolism and decreased cholinergic functioning of the central nervous system resulting in more serious side effects in the elderly. Pharmacologic treatment of anxiety and of memory impairment in the aging is discussed. Dangers of polypharmacy for the elderly are indicated. Implications for clinical practice are considered. 31 references.

002630 Sanders, W. L. Warwick Hospital, Lakin Road, Warwick CV34 5BW, England **Creutzfeldt-Jakob disease treated with amantadine.** *Journal of Neurology, Neurosurgery, and Psychiatry*. 42(10):960-961, 1979.

A case of Creutzfeldt-Jakob disease is reported in which treatment with amantadine resulted in considerable initial improvement, followed by a period of almost 5 years during which the patient remained in a relatively stable condition until he died accidentally. The diagnosis was confirmed histologically. Previous cases of Creutzfeldt-Jakob disease are discussed in which the patient was very ill and dying when treatment with amantadine was started and in which response to treatment was immediate and followed a similar pattern. It is posited that cases such as the one reported which have recovered after treatment may be another source of infection from which man to man transmission can occur. 3 references. (Author abstract modified)

002631 Schlenoff, David. Veterans Administration Medical Center, Perry Point, MD **The mentally restored client on antipsychotic medication: counselor considerations.** *Rehabilitation Literature*. 40(9):275-277, 1979.

The role of the rehabilitation counselor in helping the discharged psychiatric patient in adjusting to posthospital life is discussed. Several suggestions are offered for assisting the client to maintain his prescribed doses of antipsychotic medication. In addition the counselor must watch for specific drug side-effects. Characteristics which the counselor should have in order to be effective include skills in interviewing and in communication and a basic knowledge of psychotropics. 8 references.

002632 Schoenberg, Mark; Ts'o, Timothy O. T.; Meisel, Alan N. 201 E. Broadway, Port Jefferson, NY 11777 **Graves' disease manifesting after maintenance lithium.** *Journal of Nervous and Mental Disease*. 167(9):575-577, 1979.

A case of Graves' disease occurring at the cessation of lithium therapy is presented. A 36-year-old woman with no prior history of thyroid dysfunction developed Graves' disease (hyperthyroidism with exophthalmos) 4 months after her maintenance lithium therapy was stopped. Although a causal relationship between these events cannot be established, several hypotheses are presented. The possibility that lithium may mask the hyperthyroidism of Graves' disease but allow the exophthalmos to develop cryptically is discussed. Hyperthyroidism and mania have similar symptoms, but in the case presented two psychiatrists were able to distinguish between these two conditions by careful examination. 14 references. (Author abstract modified)

002633 Schooler, Nina R. Psychopharmacology Research Branch, NIMH, Room 10C-06, 5600 Fishers Lane, Rockville, MD 20857 **Neuroleptics and psychosocial treatments: a discussion.** *Schizophrenia Bulletin*. 6(1):131-134, 1980.

Designs of clinical trials that will permit evaluation of independent, additive, and interactive effects of drugs and psychoso-

cial treatments of schizophrenia are described. The central feature of such designs is that they incorporate control conditions for both classes of treatment. Data are presented to support the contention that the current state of knowledge in both drug and psychosocial treatment research makes such studies ethically and scientifically possible and highly desirable clinically. 16 references. (Author abstract)

002634 Schou, Mogens. Psykofarmakologisk Institut, Psykiatrisk Hospital, DK-8240 Risskov, Denmark **Bibliography on the biology and pharmacology of lithium. 6.** Neuropsychobiology. 5(5):241-265, 1979.

A bibliography including references to all aspects of the biology, pharmacology, toxicology, and clinical use of lithium, which covers the period from 1976/77 to 1977/78, is presented. Excluded from the bibliography are studies on lithium effects on bacteria and plants, studies on lithium interference with morphogenesis in lower organisms, and studies in which lithium was used merely as an aversive agent in conditioning experiments. Most of the papers listed contained original data. Textbooks and congress abstracts are listed only occasionally. The bibliography is the fifth in a series which covers the period from 1969 to the present and follows the same lines as its predecessors.

002635 Schou, Mogens. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Psychiatric Hospital, DK-8240 Risskov, Denmark **Lithium prophylaxis: is the honeymoon over?** Australian and New Zealand Journal of Psychiatry. 13(2):109-114, 1979.

After 10 to 15 years of lithium treatment for bipolar depression, lithium treatment is examined to determine whether the treatment is still seen as effective, whether any reasonable prophylactic alternative exists, and whether, although side-effects may be troublesome, they are reversible and do not endanger the patient's life. Research is reviewed which shows that lithium is efficacious, that is, significantly better than placebo; however, the quantitative efficacy of long-term lithium treatment is not definitively shown. Lithium is determined to be more effective than antidepressants, the available alternative, in cases of bipolar illness, although the two treatments are equally good or lithium somewhat better in unipolar cases. A study in progress is reviewed with regard to the question of side-effects and functional changes with lithium treatment. The observation of morphological changes in the kidneys of patients given long-term lithium treatment is concluded to be reason for further research, but not for panic. 27 references.

002636 Schou, Mogens. Psykofarmakologisk Institut, Psykiatrisk Hospital, DK-8240 Risskov, Denmark **Bibliography on the biology and pharmacology of lithium. 7.** Neuropsychobiology. 6(1):1-28, 1980.

A bibliography which includes references to all aspects of the biology, pharmacology, toxicology, and clinical use of lithium is presented. The bibliography covers the period 1977 to 1979 and contains a list of books and major reviews on lithium. Excluded are studies on lithium effects on bacteria and plants, studies on lithium interference with morphogenesis in lower organisms, and studies in which lithium was used merely as an aversive agent in conditioning experiments. Most of the papers listed contain original data; textbooks and congress abstracts are listed only occasionally.

002637 Schulz, Clarence G. Sheppard and Enoch Pratt Hospital, Towson, MD 21204 **Discussion of neuroleptics and psychosocial treatment.** Schizophrenia Bulletin. 6(1):135-138, 1980.

The Neuroleptics and Psychosocial Treatment issue of the Schizophrenia Bulletin is discussed from the viewpoint of a practicing clinician.

The clinical implications of each of the review articles are assessed in turn, and conclusions derived from the articles are summarized. In general, it is suggested that the schizophrenic patient be treated in a setting that allows one to postpone administering neuroleptics, provides alternative means of responding to intolerably disturbed or regressed behavior, emphasizes responsive, involved staff, and presents expectations of the patient's highest potential level of functioning. Efforts should be made to restore coping functions, improve family relationships, and provide a community support system. Medications should be available if necessary, used in the smallest amounts needed, and for the shortest period of time. The maintenance of a human relationship is essential to the welfare of the schizophrenic patient. 7 references. (Author abstract modified)

002638 Seppala, T.; Linnoila, M.; Mattila, M. J. Dept. of Pharmacology, University of Helsinki, Siltavuorenpenger 10 A, SF-00170, Helsinki 17, Finland **Drugs, alcohol and driving.** Current Therapeutics. 20(4):133-135, 138, 141-143, 145-146, 148-152, 1979.

The influence of alcohol and drug use and alcohol/drug interactions on driving skills and behaviors is examined in a review of laboratory and epidemiological studies for a variety of drug groups, particularly psychotropics. Drug groups discussed include: anti-anxiety drugs, hypnotics, antipsychotic drugs, lithium, antidepressants, stimulants, cannabis, hallucinogens, analgesics, anesthetics, muscle relaxants, anticholinergic drugs, antiepileptic and anti-Parkinsonian drugs, sex steroids, and other drugs such as antibiotics, cardiovascular drugs, and antihistamines. Emphasis is on drug effects on psychological, psychomotor, and perceptual performance.

002639 Shader, Richard I., Greenblatt, David J. New England Medical Center Hospital, 171 Harrison Ave., Boston, MA 02111 **Clinical indications for plasma level monitoring of psychotropic drugs.** American Journal of Psychiatry. 136(12):1590-1591, 1979.

Guidelines are presented to aid in the decision of whether to monitor plasma concentrations of psychotropic drugs. It is reported that serum levels should be monitored for drugs with narrow therapeutic ranges, when toxicity may be confused with disease symptoms, for drugs to which a pharmacokinetic tolerance develops, for drugs with poor absorption, for drugs with a therapeutic window, where the relation between parent drug and metabolite levels influences clinical response, when the drug is used for minimum maintenance, when evaluation of pharmacokinetic consequences of drug interactions is desired, when malabsorption is suspected in an individual patient, for special patient populations, to evaluate compliance, in nonresponsive patients, and in overdose management. 3 references.

002640 Shepherd, Michael. Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, England **Psychotropic drugs and taxonomic systems.** Psychological Medicine. 10(1):25-33, 1980.

Attempts to underpin the classification of psychotropic drugs in biological and clinical terms are discussed with reference to their values and limitations. Among biological classificatory systems are those based on pattern recognition methods, structure/activity correlations, and on drug effects on brain receptors, particularly dopamine receptors. Among clinical classificatory schemes are those based on the specific disorder the drug group is used to treat and/or the mechanism/site of action and adverse effects/potency. Thus, there are a variety of classification systems, each designed for a different purpose: scientific enquiry, clinical practice, didactic teaching, public communication, and reporting on side-effects. An adequate assessment of their value would appear to depend on what is demanded from each within

its own frame of reference rather than by reference to any holistic schema. The current need for a multiplicative, heuristic taxonomy is suggested. 40 references. (Author abstract modified)

002641 Snow, Lorraine Luke. University of Rhode Island *The relationship between analgesia, hypnotic susceptibility, and chronic pain intensity.* (Ph.D. dissertation). Dissertation Abstracts International. 40(2):937-B, 1979. Ann Arbor, Univ. Microfilms No. 7915471, 74p., 1978.

The effects of rapid (hypnotic) induction analgesia (RIA) and an oral placebo on clinical and experimental pain were compared in 30 volunteer male paraplegic veterans with chronic pain syndrome, and the relationship between hypnotic susceptibility, chronic pain experience, and the effect of RIA and clinical and experimental pain was investigated. Self-ratings of clinical pain were obtained before and after RIA and placebo treatments. Threshold and tolerance for ischemic muscle pain (experimental pain) were measured during baseline control, RIA, and placebo sessions. Results indicate that the effectiveness of a single RIA session for the control of clinical and experimental pain in chronic pain patients is more limited than might be anticipated from previous reports. (Journal abstract modified)

002642 Spohn, Herbert E.; Fitzpatrick, Timothy. Menninger Foundation, Box 829, Topeka, KS 66601 *Informed consent and bias in samples of schizophrenic subjects at risk for drug withdrawal.* Journal of Abnormal Psychology. 89(1):79-92, 1980.

The effect of informed consent screening on the findings of research in which schizophrenic patients are withdrawn from antipsychotic medication in order to eliminate the influence of drug treatment on dependent variables was studied. In order to determine the representativeness of a consenting sample of Ss, comparison was made to patients who did not participate in the research (no contact, refused by ward, and refused by self). Four-hundred-twenty patients were screened for informed consent by both ward personnel and themselves, and 115 consented. Multivariate analyses of variance involving a multivariate vector on which 12 demographic, organismic, and course of illness variables were massed indicates that the final consenting sample differed significantly from the reference population from which it was drawn. Multiple regression analysis indicated that early relapsing, drug withdrawn patients differed significantly in prewithdrawal characteristics from later relapsing patients. The reference population for the study was based on a previous study (Spohn et al., 1977). 16 references. (Author abstract modified)

002643 Stein, Marsha K.; Downing, Robert W.; Rickels, Karl. Dept. of Psychiatry, 203 Piersol Building, University Hospital, 3400 Spruce St., Philadelphia, PA 19104 *The Minnesota Multiphasic Personality Inventory in predicting response to pharmacotherapy of neurotic outpatients.* Journal of Nervous and Mental Disease. 167(9):542-547, 1979.

The utility of the MMPI in predicting treatment response to pharmacotherapy for a group of 54 anxious and 43 depressed outpatients was examined. Discriminant function analyses using the MMPI scales were conducted on groups of improved and unimproved patients. Several significant function, as well as zero order, differences were found. In general, improved patients scored significantly lower on scales reflecting depression and obsessive-compulsive or schizoid tendencies. They also obtained lower scores on scales measuring interpersonal sensitivity. These scores are suggestive of character traits such as low frustration tolerance, impulsivity, and resentment toward authority figures. 12 references. (Author abstract modified)

002644 Strzyzewski, Włodzimierz; Brzezinski, Jerzy. Katedra i Klinika Psychiatrii AM, ul. Szpitalna 27/33, 60-572 Poznań,

Poland /*Methodological aspects of selection of groups of patients for studies of psychotropic drugs.* Metodyczne aspekty doboru grup chorych do badań leków psychotropowych. Psychiatria Polska. 13(2):161-164, 1979.

Methods of selecting patient groups as probands for evaluating the effects of psychotropic drugs are discussed. One of the basic conditions for evaluation is to have a plan of study in which the hypotheses can be verified by appropriate statistical tests. Such a plan must satisfy three requirements: the tests must be able to be repeated, the groups of patients used for testing must be homogenous, and they must be selected at random, because the placebo method cannot be used, especially in tests of antidepressants. It is concluded that in view of the above principles, a retrospective evaluation of psychotropic drugs is least appropriate, since such comparative tests involve errors which are difficult to determine and therefore, cannot lead to any valid statistical conclusions. 11 references.

002645 Swett, Chester, Jr. Dept. of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178 *Patterns of drug use in psychiatric inpatient wards.* Journal of Clinical Psychiatry. 40(11):464-468, 1979.

Patterns of drug use over a 6 year period were monitored in 2,593 psychiatric inpatients in six hospitals. The efficacy was rated as satisfactory in 78% of the drug exposures. Nearly 37% of the patients showed an adverse reaction. However, only 1.5% of the reactions were of major severity. Distribution of patients, diagnostic data, indications for drug therapy, drugs most commonly used, characteristics of adverse drug reactions, demographic data for patients with adverse reactions, and the duration of hospitalization and adverse drug reaction are also presented. 6 references. (Author abstract modified)

002646 Tamir, Ilana; Mechoulam, Raphael; Meyer, Amatzya Y. Dept. of Natural Products, School of Pharmacy, Hebrew University, Jerusalem, Israel *Cannabidiol and phenytoin: a structural comparison.* Journal of Medicinal Chemistry. 23(2):220-223, 1980.

Conformational energy maps have been computed for the antiepileptic agents phenytoin and cannabidiol by the quantum-mechanical method of perturbative configuration interaction with localized orbitals (PCILO). The computation indicates that the spatial relationship between the two rings in the two drugs is similar and close to the respective structures in the crystal. This is supported by ¹H and ¹³C NMR measurements. Hence, both compounds fulfill the stereochemical requirements suggested for anticonvulsant drug action. 28 references. (Author abstract)

002647 Towery, O. B.; Brands, Alvira B. Office of Program Planning and Evaluation, Alcohol, Drug Abuse, and Mental Health Administration, Rockville, MD 20857 *Psychotropic drugs: approaches to psychopharmacologic drug use.* Washington, DC, GPO, 1979. 71 p.

Approaches to psychopharmacologic drug use are examined in an attempt to enhance the capacity of community mental health centers to develop their own quality assurance programs for psychotropic compounds. Guidelines for drug use review in mental health facilities, prepared by a multidisciplinary group of pharmacists, pharmacologists, psychiatrists, social workers, and registered nurses are first presented. A set of psychopharmacologic screening criteria for use by peer review groups and developed by a subcommittee of the Peer Review Committee of the American Psychiatric Association is then provided.

002648 Vartanian, F. E. Division of Mental Health, World Health Organization, CH-1211 Geneva 27, Switzerland World

Health Organization Activity in Psychopharmacotherapy. Progress in Neuro-Psychopharmacology. 3(1-3):5-9, 1979.

The efforts of the World Health Organization (WHO) in the area of psychopharmacology are reviewed. It is noted that the Division of Mental Health of WHO is developing a series of closely linked activities concerned with research, information exchange, and training in biological psychiatry, including psychopharmacology. One of the main mechanisms utilized in WHO programs is joint work in a network of collaborating centers. These collaborating centers are distributed world wide, and carry out projects on clinical psychopharmacology and biological psychiatry. It is contended that the successful development of these collaborative activities has created the optimal conditions for international collaboration toward rational treatment approaches to mental disorders. 6 references. (Author abstract modified)

002649 Vencovsky, Eugen; Dobias, Jan. Regional Institute of Public Health, Plzen, Czechoslovakia **Remarks on pharmacotherapy of functional psychoses.** Socijalna Psihijatrija. 7(1):77-82, 1979.

The history of clinical psychopharmacology is traced and benefits of this approach are discussed. It is suggested that psychopharmacotherapy has humanized psychiatric therapy, accelerated in an outstanding way the compensation of the mental disease, and has helped to establish a valuable psychotherapeutic contact with the mental patients. Psychopharmacotherapy affords the mental patients the possibility of at least a relative recovery, and it often affords mental patients full return to their former lifestyle. Psychopharmacotherapy has entirely removed the former era of mere care in psychiatry, which did not treat mental patients but merely cared for them. Psychotherapy and sociotherapy have been joined by a further most significant method of psychiatric therapy, pharmacotherapy. It is an inseparable component in the complex therapy for mental patients. (Journal abstract modified)

002650 Ward, L. Charles. Dept. of Psychiatry, Medical College of Georgia, Augusta, GA 30912 **Comment on Journal of Consulting and Clinical Psychology.** 47(5):975-976, 1979.

The conclusions of the Rie & Rie in a 1977 study on the ability of Ritalin to enhance story recall are questioned. Rie and Rie concluded that Ritalin enhances story recall after a 2 hour retention interval but not after 2 days and that the lack of difference in later recall argues against a facilitation of scholastic achievement due to Ritalin. The former conclusion is questionable because of inappropriate statistical analyses and because of the effects of confoundings contained in the experimental design. The latter conclusion appears to arise from the misconception of equating achievement with long-term memory independently of amount learned. It is concluded that achievement is a function of both learning and memory, and the distinction should be maintained in examining Ritalin's effects. 2 references. (Author abstract)

002651 Weal, Elizabeth. American Institutes for Research, P. O. Box 1113, Palo Alto, CA 94302 **A medical education program for psychiatric patients being discharged to the community./Released patients get meds education.** Innovations. 6(2):37, 1979.

A discharge program for psychiatric patients returning to the community which features medical education, discussion of the nature of outpatient care, and a discharge instruction sheet, is described. Prior to discharge, patients are told about the medications and plans for future treatment. Specifically, the patient is told the trade name, generic name, and classification (i.e., antipsychotic, antidepressant, antianxiety agent, antispasmodic agent) of the drug, precautions to consider when taking the medication,

telephone number, and name of the doctor to call if side-effects are experienced, the number of days medication supplied, and general safety precautions regarding storage of the medication.

002652 Weiner, Richard D.; Henschen, Gary M.; Dellasega, Mark; Baker, John S. Durham Veterans Administration Medical Center, 508 Fulton St., Durham, NC 27705 **Propranolol treatment of an ECT-related ventricular arrhythmia.** American Journal of Psychiatry. 136(12):1594-1595, 1979.

The treatment of a case of cardiac complications from ECT is reported. A 62-year-old man suffering from severe depression with vegetative symptoms was treated with ECT. He had no history of cardiac disease. The patient received 10 ECT treatments with no signs of respiratory distress or cyanosis. Several minutes after the first treatment, a sinus tachycardia developed concurrently with signs of arousal. A course of propranolol was started and the dosage increased until the postictal tachycardia ceased to occur. The last seven treatments were administered without incident. It is suggested that the cardiac arrhythmia resulted from the autonomic stress associated with postictal arousal and heightened anxiety. 7 references.

002653 Werry, John S. Dept. of Psychiatry, University of Auckland School of Medicine, Auckland, New Zealand **Principles of use of psychotropic drugs in children.** Current Therapeutics. 20(10):45-46, 49-52, 1979.

Aspects of psychotropic drug treatment in children are examined and the need for a more medical and scientific approach to its use in this population is emphasized. Topics include the importance of an objective diagnosis; the different categories of psychotherapeutic compounds (stimulants, antipsychotics, antidepressants, anxiolytics and sedatives, and anticonvulsants); and assessment of adverse effects. It is concluded that only the stimulants have a well tested place in pediatric psychopharmacology and then only on specialist approval. Unanswered questions remain, including the degree to which stimulants influence long-term prognosis and the effect of changes in cognitive function and on academic achievement.

002654 Wieck, H. H.; Heerklotz, Brigitte. Universitäts-Nervenkranklinik im Kopfklinikum Erlangen, Schwabachanlage 6 u 10, D-8520 Erlangen, Germany **The mode of action of modern tranquilizers from the benzodiazepine group: a clinical view.** Journal of International Medical Research. 7(6):573-582, 1979.

The mode of action of modern benzodiazepine tranquilizers is examined, with emphasis on the development of a diagnostic and therapeutic interaction between the indication of general psychovegetative disorders and the mode of action of the modern ataractics. The clinical indications for tranquilizers are delineated, followed by the ideal properties of an effective tranquilizer. Indications for the various compounds are reviewed, and the clinical position of clobazam is briefly discussed. 38 references.

002655 Yosselson-Superstine, Shimona; Sternik, D.; Liebenzon, D. Dept. of Pharmacy, School of Pharmacy, Hebrew University, Jerusalem, Israel **Prescribing patterns in psychiatric hospitals in Israel.** Acta Psychiatrica Scandinavica. 60(5):477-482, 1979.

A survey was conducted by pharmacists working in four psychiatric hospitals in Israel in order to assess the prescribing of psychotropic drugs. Polypharmacy was found to be common. Patients were receiving up to 11 different drugs and up to six different psychotropic drugs. The average number of psychotropic drugs per patient was two. The most popular combinations of drugs used were: an antipsychotic drug and an antiparkinsonian drug, and a combination of more than one antipsychotic agent. Up to 30 doses per day were taken orally by one patient.

Drugs that could have easily been administered on a once daily schedule were often administered several times a day. Differences in prescribing patterns in the various hospitals and wards of the same institution could more easily be attributed to differ-

ent educational backgrounds, habits, personal beliefs, and experience rather than to the types of patients treated. 13 references. (Author abstract)

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